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619. *The Stability Constants of the Silver Complexes of Some* NN-*Substituted 2-Hydroxyethylamines.*

By D. J. Alner and R. C. Lansbury.

Stability constants for the silver complexes of the *NN*-dimethyl, *NN*-diethyl, and *NN*-di-isopropyl derivatives of 2-hydroxyethylamine have been obtained at 20° by electrode-potential and solubility measurements. In addition, the basic dissociation constants have been determined.

There being no published values for the dissociation constants of *NN*-dimethyl, *NN*-diethyl, and *NN*-di-isopropyl derivatives of 2-hydroxyethylamine, or for the stability of their silver complexes, we have remedied this deficiency.

Experimental

Dissociation Constants of the NN-*Substituted 2-Hydroxyethylamines at* 20°.—The compounds were purified by distillation under reduced pressure and characterised by measurement of refractive indices (Hilger–Chance Refractometer) and equivalent weight (see Table 1).

Table 1. *Properties of* NN-*substituted 2-hydroxyethylamines.*

	Dimethyl		Diethyl		Di-isopropyl	
	Found	Lit.	Found	Lit.	Found	Lit.
Purity (% as base)	98·7		99·7		99·9	
n_D^{20}	1·4296	1·4300 [1]	1·4412	—	1·4428	—
n_D^{25}	1·4276	—	1·4388	1·4400,[2] 1·4389 [3]	1·4408	—

Dissociation constants were determined by measuring the pH values set up during neutralisation of the base in the cell;

$$Pt,H_2(1\ atm.)\ |\ Base + HCl\ |\ Sat.\ KCl\ bridge\ |\ Sat.\ calomel$$

Dilute solutions of the bases were titrated with hydrochloric acid at 20°, and from the measured e.m.f.s the pH values were calculated, where pH is defined by $pH = -\log\{H^+\}$ (braces denote activities). The calomel electrode potential was taken [4] as 0·2476 v at 20°. Titration data are

Table 2. *Dissociation constants at* 20° *of* NN-*substituted 2-hydroxyethylamines.*

Dimethyl			Diethyl			Di-isopropyl		
HCl (ml.)	pH (obs.)	p*K*	HCl (ml.)	pH (obs.)	p*K*	HCl (ml.)	pH (obs.)	p*K*
(i) 50 ml. *of* 0·0505M-*base titrated with* 0·497M-HCl			(i) 50 ml. *of* 0·0504M-*base titrated with* 0·497M-HCl			(i) 50 ml. *of* 0·487M-*base titrated with* 0·497M-HCl		
1·00	9·96	4·87	1·00	10·52	4·29	1·00	10·72	4·07
1·50	9·74	4·86	1·50	10·31	4·29	1·50	10·50	4·07
2·00	9·56	4·86	2·00	10·12	4·29	2·00	10·32	4·07
2·50	9·39	4·86	2·50	9·96	4·29	2·50	10·14	4·08
3·00	9·23	4·85	3·00	9·79	4·29	3·00	9·97	4·07
3·50	9·03	4·87	3·50	9·61	4·29	3·50	9·77	4·08
4·00	8·81	4·87	4·00	9·38	4·30	4·00	9·51	4·09
	Mean	4·86		Mean	4·29		Mean	4·08
(ii) 50 ml. *of* 0·0101M-*base titrated with* 0·105M-HCl			(ii) 50 ml. *of* 0·101M-*base titrated with* 0·105M-HCl			(ii) 50 ml. *of* 0·00974M-*base titrated with* 0·0998M-HCl		
1·00	9·88	4·88	1·00	10·40	4·33	1·00	10·60	4·11
1·50	9·66	4·87	1·50	10·20	4·31	1·50	10·41	4·10
2·00	9·48	4·86	2·00	10·03	4·31	2·00	10·24	4·09
2·50	9·30	4·86	2·50	9·85	4·31	2·50	10·07	4·10
3·00	9·11	4·87	3·00	9·67	4·31	3·00	9·87	4·10
3·50	8·90	4·87	3·50	9·46	4·31	3·50	9·68	4·11
	Mean	4·87		Mean	4·31		Mean	4·10

[1] Knorr and Mathes, *Ber.*, 1901, **34**, 3482.
[2] Horne and Schriener, *J. Amer. Chem. Soc.*, 1932, **54**, 2928.
[3] Headlee, Collet, and Lazzell, *J. Amer. Chem. Soc.*, 1933, **55**, 1066.
[4] Bates, "Electrometric pH Determinations," Chapman & Hall, London, 1954, p. 201.

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TABLE 3. *Solubility of silver hydroxide at 20° in* NN-*substituted 2-hydroxyethylamines.*

Dimethyl			Diethyl			Di-isopropyl		
Base (10^{-2}M)	AgOH (10^{-4}M)	log β_2	Base (10^{-2}M)	AgOH (10^{-4}M)	log β_2	Base (10^{-2}M)	AgOH (10^{-4}M)	log β_2
10·1	7·1	3·88	10·1	18·6	4·64	4·3	1·2	3·93
15·1	12·1	3·89	15·1	28·3	4·59	6·5	1·7	3·82
20·2	16·1	3·85	20·1	44·5	4·66	8·6	2·4	3·78
25·2	20·3	3·82	25·2	56·3	4·64		Mean	3·84
30·3	24·5	3·80	30·2	68·1	4·63			
35·3	29·0	3·79	35·2	80·1	4·62			
40·4	33·8	3·79	40·3	90·5	4·59			
	Mean	3·83		Mean	4·62			

TABLE 4. *Titration of* NN-*substituted 2-hydroxyethylamines* (50 ml. *portions*) *with silver nitrate at 20° in presence of* HNO_3 (10 ml.).

Dimethyl				Diethyl				Di-isopropyl			
$AgNO_3$ (ml.)	pH (obs.)	pAg (obs.)	log β_2	$AgNO_3$ (ml.)	pH (obs.)	pAg (obs.)	log β_2	$AgNO_3$ (ml.)	pH (obs.)	pAg (obs.)	log β_2
Base 0·0503M; HNO_3 0·0508M; $AgNO_3$ 0·0100M				Base 0·0496M; HNO_3 0·0508M; $AgNO_3$ 0·0100M				Base 0·0424M; HNO_3 0·101M; $AgNO_3$ 0·0050M			
3·00	9·73	4·261	3·85	3·00	10·32	5·047	4·71	2·00	10·18	4·561	4·12
4·00	9·71	4·100	3·82	4·00	10·31	4·907	4·71	2·50	10·17	4·550	4·11
5·00	9·70	3·993	3·82	5·00	10·31	4·794	4·71	3·00	10·17	4·343	4·08
6·00	9·70	3·903	3·83	6·00	10·29	4·684	4·69	3·50	10·17	4·270	4·08
7·00	9·69	3·828	3·83	7·00	10·28	4·605	4·69	4·00	10·17	4·211	4·08
8·00	9·69	3·762	3·83	8·00	10·27	4·533	4·69	4·50	10·17	4·161	4·09
9·00	9·68	3·707	3·84	9·00	10·26	4·466	4·69	5·00	10·16	4·122	4·10
10·00	9·68	3·654	3·84	10·00	10·25	4·409	4·70			Mean	4·09
11·00	9·67	3·606	3·85	11·00	10·25	4·353	4·70				
12·00	9·67	3·561	3·85	12·00	10·25	4·308	4·70				
		Mean	3·84			Mean	4·70				
Base 0·201M; HNO_3 0·102M; $AgNO_3$ 0·050M				Base 0·199M; HNO_3 0·200M; $AgNO_3$ 0·050M				Base 0·0849M; HNO_3 0·101M; $AgNO_3$ 0·0100M			
3·00	10·12	4·739	3·77	6·00	10·30	5·122	4·61	2·00	9·76	4·211	4·03
4·00	10·11	4·585	3·75	8·00	10·30	4·968	4·61	2·50	9·76	4·105	4·02
5·00	10·10	4·464	3·74	10·00	10·28	4·842	4·62	3·00	9·75	4·025	4·03
6·00	10·09	4·372	3·75	12·00	10·26	4·731	4·63	3·50	9·75	3·953	4·03
7·00	10·08	4·290	3·75	14·00	10·25	4·631	4·63	4·00	9·75	3·891	4·03
8·00	10·07	4·224	3·76	16·00	10·23	4·534	4·63	4·50	9·74	3·840	4·04
9·00	10·06	4·158	3·76	18·00	10·21	4·448	4·63	5·00	9·74	3·795	4·04
10·00	10·06	4·099	3·76	20·00	10·19	4·370	4·64			Mean	4·03
11·00	10·04	4·032	3·75			Mean	4·63				
12·00	10·03	3·982	3·75								
		Mean	3·75								

recorded in Table 2, where K refers to the equilibrium $B + H_2O \rightleftharpoons BH^+ + OH^-$, being defined by $K = \{BH^+\}\{OH^-\}/\{B\}$, where $\{BH^+\} = ([HCl] - [H^+] + [OH^-])f_\pm$, and $\{B\} = ([\text{Total base}] - [HCl] + [H^+] - [OH^-])\ f_\pm$(square brackets denote concentrations in mole/l.). The mean activity coefficients of the univalent ionic species in solution were calculated from the relation [5] $-\log f_\pm = 0{\cdot}505\sqrt{I}/(1 + \sqrt{I})$, where I = ionic strength. The activity coefficient of the un-ionised, uncombined base was taken as unity. Temperature control was maintained within $\pm 0{\cdot}1°$. The basic dissociation constants of the *NN*-substituted 2-hydroxyethylamines recorded in the present investigation are new.

Solubility of Silver Hydroxide in Aqueous Solutions of the NN-*Substituted 2-Hydroxyethylamines at* 20°.—Silver hydroxide was prepared by precipitation from 0·1M-silver nitrate by addition of the stoicheiometric amount of 0·1M-sodium hydroxide (carbonate free). It was washed free from extraneous ions. An excess of the moist silver hydroxide was added to standard aqueous solutions of the bases and equilibrated at 20° under air-free conditions in black bottles. The solutions were filtered from silver hydroxide and analysed for their total silver contents by Volhard's thiocyanate method (see Table 3).

[5] Guggenheim and Schindler, *J. Phys. Chem.*, 1934, **38**, 539.

Titration of Aqueous Solutions of NN-*Substituted* 2-*Hydroxyethylamines with Silver Nitrate.*— To prevent the immediate precipitation of silver hydroxide in this titration, known volumes of standard nitric acid were added to amine solutions of given concentration so as suitably to adjust their initial pH values. These solutions were then progressively titrated with standard solutions of silver nitrate at 20°. The titrations were carried out in a black beaker, since the complexes were light-sensitive.

A glass electrode was used to record the pH values, and silver iodide electrodes for the pAg values during titration of the base in the cell:

$$\text{Ag} \,|\, \text{AgI Glass elec.} \,|\, \text{Base} + \text{HNO}_3 + \text{AgNO}_3 \,|\, \text{Sat. KNO}_3 \text{ bridge} \,|\, \text{Sat. calomel}$$

Silver electrodes were unsuitable, as they did not function reversibly in these solutions. Silver iodide electrodes have been employed by other workers [7] to determine $\{Ag^+\}$. Nitrogen was bubbled through the whole to effect mixing and exclude carbon dioxide. The pH and pAg values of the silver iodide–calomel cell, together with the calculated stability constants, are recorded in Table 4.

Discussion

The mechanism for complex formation between the *NN*-disubstituted 2-hydroxyethylamines and silver hydroxide has been represented [6] in terms of the formation of strong complex bases of the type AgB_nOH, where B is the ligand; thus $AgOH + nB \rightleftharpoons AgB_nOH = AgB_n^+ + OH_C^-$. The complex cation AgB_n^+ must be in equilibrium with silver ions $AgB_n^+ \rightleftharpoons Ag^+ + nB$, its stability constant being defined by $\beta_n = \{AgB_n^+\}/\{Ag^+\}\{B\}^n$. The uncombined base present in the complex solution will ionise ($B + H_2O \rightleftharpoons BH^+ + OH_B^-$); and the solution conditions must also satisfy the solubility product relation for silver hydroxide at 20°, *viz.*, $K_s = \{Ag^+\}\{OH^-\}_{B+C}$, since the solution was saturated with respect to silver hydroxide. The subscripts B and C denote the source of the hydroxyl ions. From the solubility product relation the activity of the silver ions in the equilibrium mixture may be calculated, provided $\{OH^-\}_{B+C}$ is known.

If s equiv./l. represents the concentration of silver found by analysis we can equate this to the concentration of the complex cation AgB_n^+, since under the experimental conditions (where large excesses of the base were present) dissociation of the complex cation could be assumed to be negligibly small. If c equiv./l. represents the initial concentration of base, then the concentration of the uncombined, un-ionised base in the equilibrium solution is $(c - ns - [OH^-]_B)$. The stability constant expression becomes:

$$\beta_n = \frac{sf^2[OH^-]_{B+C}}{K_s(c - ns - [OH^-]_B)}, \qquad (1)$$

where f represents the mean activity coefficient, and the activity coefficient of the un-ionised base is taken as unity

The hydroxyl-ion concentration arising from the ionisation of the base was calculated from a knowledge of the respective dissociation constant, *i.e.*,

$$K = \{BH^+\}\{OH^-\}_{B+C}/\{B\} \qquad (2)$$

Since $[BH^+] = [OH^-]_B = x$ (say), and $[AgB_n^+] = [OH^-]_C = s$, equation (2) becomes

$$K = \frac{xf^2(x + s)}{(c - ns - x)}. \qquad (3)$$

A first approximation for the value of the activity coefficient was calculated on the assumption that the ionic strength was equal to the concentration of the complex base AgB_nOH. Substitution of this value into equation (3) enabled the quadratic in x to be solved, on the assumption that $n = 2$. Corrected values for the ionic strength $I = (s + x)$ and for the activity coefficient were evaluated, and successive approximations

[6] Alner and Smeeth, *J.*, 1958, 852, 4207.
[7] Antikainen, Heitanen, and Sillén, *Acta Chem. Scand.*, 1960, **14**, 95.

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were repeated until constant values for f and x were obtained. Substitution of these values into equation (1) permits calculation of the stability constant, it being assumed that $n = 2$. It was shown that n possessed this value by graphically representing $f\sqrt{s(s+x)}$ values against $(c - 2s - x)$ values: straight lines passing through the origin were obtained. Values for log β_2 calculated from equation (1) are recorded in Table 3. The value for K_a was taken [6] as $1{\cdot}413 \times 10^{-8}$ at 20°.

Throughout the titrations with silver nitrate, a large excess of base was present, justifying the assumption that the complexes were present in solution in their limiting forms, AgB_2^+. pAg measurments were taken as representing activities of the free silver ions in the equilibrium solutions.

If s equiv./l. represents the total silver concentration (as before), and $[Ag^+]$ the concentration of free silver ions calculated from the pAg values and mean activity coefficients, the concentration of the complex is $(s - [Ag^+])$ and that of the uncombined, un-ionised base is $\{c - 2(s - [Ag^+]) - [OH^-]\}$. Thus the stability constant expression becomes:

$$\beta_2 = \frac{(s - [Ag^+])}{\{c - 2(s - [Ag^+]) - [OH^-]\}[Ag^+]}, \qquad (4)$$

since activity coefficients cancel. Table 4 records the calculated values of log β_2 for the complexes investigated, determined by direct substitution of the experimental results into equation (4).

For each complex, the values of the stability constant obtained by the two methods were in good agreement.

The dissociation constants demonstrate the order of basic strengths to be di-isopropyl > diethyl > dimethyl, but the stability values of the complexes do not show the same regular gradation.

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620. *π-Cyclopentadienyl- and Cyclopentadiene-iron Carbonyl Complexes.*

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Chloro-π-cyclopentadienyldicarbonyliron has been converted by the action of carbon monoxide and triphenyl-phosphine, -arsenine, or -stibine into the cationic species π-$C_5H_5Fe(CO)_3^+$ and $[\pi$-$C_5H_5Fe(CO)_2MPh_3]^+$ (where M = P, As, or Sb).

Reduction by sodium borohydride of the triphenylphosphine-substituted ion gives dicarbonylcyclopentadienetriphenylphosphineiron, but the tricarbonyl cation gives only hydridodicarbonyl-π-cyclopentadienyliron.

Infrared and nuclear magnetic resonance spectra are reported.

THE interaction of iron pentacarbonyl with cyclopentadiene or its dimer produces the binuclear carbonyl $[\pi$-$C_5H_5Fe(CO)_2]_2$,[1] and it has been suggested [2,3] that a cyclopentadiene olefin-type complex, $C_5H_6Fe(CO)_3$, is an intermediate in the preparation. An unsuccessful attempt [4] has been made to isolate such a complex from spiro[4,4]nona-1,3-diene, but rearrangement occurred producing tetracarbonyldi-π-tetrahydroindenyldi-iron.

[1] For references see Wilkinson and Cotton, " Progress in Inorganic Chemistry," Interscience Publ. Inc., New York, 1959, Vol. I, p. 1.
[2] Sternberg and Wender, Int. Conf. Co-ordination Chem., London, 1959, *Chem. Soc. Special Publ.*, No. 13, p. 35.
[3] Pauson, *Proc. Chem. Soc.*, 1960, 297.
[4] Hallam and Pauson, *J.*, 1958, 646.

We have previously shown [5] that suitable π-cyclopentadienylmetal cations can be reduced by lithium aluminium hydride or sodium borohydride to give cyclopentadiene olefin-type complexes, *e.g.*, π-$C_5H_5CoC_5H_6$. It seemed reasonable to expect that if cations such as π-$C_5H_5Fe(CO)_3^+$ could be obtained, their reduction by hydride ion should lead to the corresponding olefin complexes;

$$\pi C_5H_5FeL_3^+ + H^- = C_5H_6FeL_3$$

π-Cyclopentadienylcarbonyliron Cations.—Cations of this type have not been reported previously, although the yellow aqueous solutions of π-$C_5H_5Fe(CO)_2Cl$ undoubtedly contain the ion $[\pi$-$C_5H_5Fe(CO)_2H_2O]^+$.[1] If the dicarbonyl chloride in acetone solution in the presence of sodium tetraphenylborate is treated with carbon monoxide under pressure, fine yellow crystals of the tetraphenylborate of the ion π-$C_5H_5Fe(CO)_3^+$ are obtained in almost quantitative yield:

$$\pi\text{-}C_5H_5Fe(CO)_2Cl + NaBPh_4 + CO = \pi\text{-}C_5H_5Fe(CO)_3[BPh_4] + NaCl$$

The tetraphenylborate decomposes only slowly in air; it is insoluble in non-polar solvents and is sparingly soluble in acetone from which it crystallises with difficulty. It decomposes without melting when heated. Conductivity measurements in nitrobenzene [6] show that it is a 1 : 1 electrolyte. The ion completes the isoelectronic series [1] $[\pi$-$C_5H_5V(CO)_3]^{2-}$, $[\pi$-$C_5H_5Cr(CO)_3]^{1-}$, π-$C_5H_5Mn(CO)_3$.

Since other ligands, particularly tertiary phosphines, could be expected to act similarly to carbon monoxide in the above reaction, we have re-examined the interaction of π-$C_5H_5Fe(CO)_2Cl$ and triphenylphosphine [7] which gave a small yield of $(Ph_3P)_2Fe(CO)_3$. This observation has been confirmed, but we have found that if the benzene-insoluble portion of the reaction mixture is extracted with water, a solution of $[\pi$-$C_5H_5Fe(CO)_2PPh_3]^+$ is obtained from which the chloride can be isolated as a trihydrate. This yellow solid decomposes without melting; it is sparingly soluble in cold water but readily soluble in hot water. Aqueous solutions give the usual precipitation reactions with large anions, and conductivity measurements in nitrobenzene showed that the chloride is a 1 : 1 electrolyte and the hexachloroplatinate(IV) a 1 : 2 electrolyte. Similar salts were characterised with triphenylarsine and triphenylstibine as ligands, but these are less stable in air than the very stable phosphine derivatives.

The infrared spectra of the isoelectronic π-cyclopentadienyl tricarbonyl compounds, $Cs_2[\pi$-$C_5H_5V(CO)_3]$, $Na[\pi$-$C_5H_5Cr(CO)_3]$, π-$C_5H_5Mn(CO)_3$, and $[\pi$-$C_5H_5Fe(CO)_3][BPh_4]$, show two strong bands due to terminal C–O stretching modes. The formal oxidation state of the metals in this series are V(−1), Cr(0), Mn(+1), and Fe(+2). The values of the C–O stretching frequencies can be interpreted as showing the degree of electron-transfer from the metal orbitals into vacant orbitals of the carbon monoxide by metal–carbon π-bonding. The stretching frequencies for this series are: 1748, 1645; 1876, 1695; 2035, 1953; [8a] and 2120, 2070 cm.$^{-1}$. These show the expected increase in π-bonding with increasing negativity of the oxidation state (Fe ⟶ V) of the central metal atom in a manner analogous to that of the N–O stretching frequencies in the isoelectronic series $K_2[Fe(CN)_5NO]$, $K_3[Mn(CN)_5NO]$, $K_5[V(CN)_5NO]$.[8b] In the triphenyl-phosphine,-arsine, and -stibine complexes the carbonyl stretching modes occur at 2070, 2030; 2062, 2017; and 2005, 2050 cm.$^{-1}$, respectively. The lowering of these values from 2120 cm.$^{-1}$ for the tricarbonyl to about 2060 cm.$^{-1}$ for the phosphorus, arsenic, and antimony compounds may be associated with decreasing π-bonding capacity here, with a resultant increase in π-bonding between

[5] Green, Pratt, and Wilkinson, *J.*, 1959, 3753.
[6] Nyholm and Morris, *J.*, 1956, 4375.
[7] Hallam and Pauson, *J.*, 1956, 3030.
[8] (*a*) Fischer, *Chem. Ber.*, 1960, **93**, 165; (*b*) Griffith, Lewis, and Wilkinson, *J.*, 1959, 1632; (*c*) Abel, Bennett, and Wilkinson, *J.*, 1959, 2323; Chatt and Hart, *J.*, 1960, 1378.

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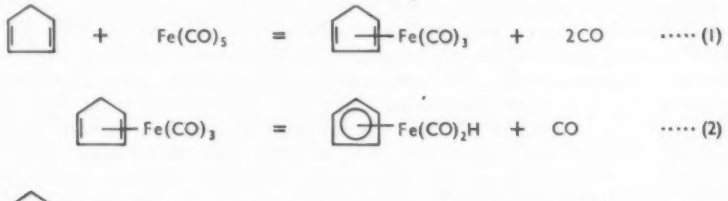
metal and carbon monoxide. The C–O frequencies increase in the order $SbPh_3 < AsPh_3 < PPh_3$ but the differences are small, *ca.* 12 cm.$^{-1}$, and are probably of little real significance except that they confirm the observations [8c] that there is little difference in π-acceptor properties of phosphorus, arsenic, and antimony as ligand atoms.

Dicarbonylcyclopentadienetriphenylphosphine iron.—Although we have failed to obtain a cyclopentadiene derivative by reduction of the ion $[\pi\text{-}C_5H_5Fe(CO)_3]^+$, reduction of the triphenylphosphine derivative, $[\pi\text{-}C_5H_5Fe(CO)_2PPh_3]Cl$, by sodium borohydride in tetrahydrofuran–ether gives the olefin-type complex, $C_5H_6Fe(CO)_2PPh_3$.

The physical and chemical properties of dicarbonylcyclopentadienetriphenylphosphine iron show that cyclopentadiene is bound to the iron atom in the same manner as in the cobalt and rhodium compounds,[5] and that the methylene group ($>CH_\alpha H_\beta$) of the cyclopentadiene has the same unusual features as before. The compound decomposes appreciably when left in air but is stable in nitrogen or *in vacuo* at room temperature. With carbon tetrachloride it reacts, to give chloroform and the $\pi\text{-}C_5H_5Fe(CO)_2PPh_3^+$ ion. In boiling xylene the compound decomposes to give $[\pi\text{-}C_5H_5Fe(CO)_2]_2$ and a small amount of ferrocene (which probably results from the decomposition of the binuclear carbonyl in xylene [7]). Interaction between the compound and triphenylmethyl tetrafluoroborate is very slow, the reactive H_α being removed essentially quantitatively to give the crystalline salt $[\pi\text{-}C_5H_5Fe(CO)_2PPh_3]BF_4$; the infrared spectrum of the latter is consistent with formulation as an ionic tetrafluoroborate.[9]

The infrared spectrum of $C_5H_6Fe(CO)_2PPh_3$ shows an intense band at 2765 cm.$^{-1}$ assignable to the C–H_α stretching mode; other assignments are also similar to those of other cyclopentadiene derivatives.[5] The high-resolution nuclear magnetic resonance spectrum is also similar in its general features to those of the other derivatives.[5] Thus there are three groups of lines in the spectrum, indicating the presence of at least three types of hydrogen atom. A sharp doublet (τ 2·73, relative intensity 15) is clearly due to the protons of the triphenylphosphine portion, the proton line being split by coupling with the ^{31}P nuclear spin. The remaining lines are assignable as before. The band at τ 4·87 (relative intensity 2) from protons on $C_{(3)}$ and $C_{(4)}$, which appears as a triplet, should exist as a double doublet due to spin-coupling of each proton with those on $C_{(2)}$ and $C_{(5)}$, but this expected fine structure was not resolvable owing to overlapping of the bands. The third band at τ 7·5 (relative intensity 4) is due to the remaining protons on the C_5H_6 group. The lines at τ 7·19, τ 7·38, and τ 8·0 appear to be part of an AB pair due to the protons of the non-equivalent methylene group, $>CH_\alpha H_\beta$; the *endo*-proton, H_α, is in a different magnetic environment from that of the *exo*-proton H_β. The poorly resolved lines at τ 7·66 and τ 7·79 are due partly to H_α and to the protons on $C_{(2)}$ and $C_{(5)}$.

Discussion.—In the interaction of cyclopentadiene with iron pentacarbonyl, the following reactions have been proposed: [2,3]



It is known that $\pi\text{-}C_5H_5Fe(CO)_2H$, which is readily obtained by the action of sodium borohydride on $\pi\text{-}C_5H_5Fe(CO)_2Cl$, is thermally unstable, decomposing in the liquid state

[9] Sharp and Sheppard, *J.*, 1957, 674.

to give the binuclear carbonyl and hydrogen.[10] However, all our attempts to isolate $C_5H_6Fe(CO)_3$ by borohydride reduction of $[\pi\text{-}C_5H_5Fe(CO)_3]^+[BPh_4]^-$ in tetrahydrofuran failed, even at low temperatures, the reaction leading only to the dicarbonyl hydride with loss of carbon monoxide. It appears that $C_5H_6Fe(CO)_3$ is unstable with respect to $\pi\text{-}C_5H_5Fe(CO)_2H$ and that the transition-state activated complex $[\pi\text{-}C_5H_5Fe(CO)_2LH]$ (L = CO) decomposes by loss of carbon monoxide in preference to forming the neutral compound $C_5H_6Fe(CO)_3$. In the case where $L = PPh_3$, only a small amount of $\pi\text{-}C_5H_5Fe(CO)_2H$, which was detected by its high-field proton-resonance line and by its decomposition to $[\pi\text{-}C_5H_5Fe(CO)_2]_2$, is produced and the main product is the neutral cyclopentadiene complex. The latter is stable with respect to ligand-loss and hydrogen-transfer to metal to give $\pi\text{-}C_5H_5Fe(CO)_2H$, and there is no evidence of decomposition below 113° to $[\pi\text{-}C_5H_5Fe(CO)_2]_2$. Although the complex $C_5H_6Fe(CO)_3$ is unstable, there appears to be no inherent instability in diolefin-iron tricarbonyl systems and tricarbonyl compounds of norbornadiene, butadiene, cycloheptadiene, etc., are known, although these compounds do not contain a reactive $\succ CH_\alpha H_\beta$ group.

The readier loss of carbon monoxide in the reduction of $\pi\text{-}C_5H_5Fe(CO)_3^+$ than in that of the triphenylphosphine complex, and similar differences in reactivities between acylcobalt carbonyls and their triphenylphosphine analogues,[11] may be due to the non-volatility of triphenylphosphine and its weaker π-bonding capacity which tends to strengthen the remaining Fe–C bonds.

Our observations thus appear to be consistent with the above reaction scheme, but further studies to elucidate the mechanism of hydrogen-transfer are in progress.

Experimental

Microanalyses and molecular weights (ebullioscopic in benzene) are by the Microanalytical Laboratories, Imperial College.

Tricarbonyl-π-cyclopentadienyliron Tetraphenylborate.—Method 1. Chlorodicarbonyl-π-cyclopentadienyliron (0·5 g.) and sodium tetraphenylborate (0·85 g.) were dissolved in anhydrous acetone (2—3 ml.). The solution was placed in a small autoclave with carbon monoxide (90 atm.; 25—30°) for 48 hr. The product crystallised in the autoclave as large golden-yellow triangular plates; these were crushed and washed with air-free water. Recrystallisation from acetone at −78° and drying in a vacuum gave the yellow *complex*, decomp. >184° (1·07 g., 85%) (Found: C, 73·3; H, 5·0; O, 9·5. $C_{32}H_{25}BFeO_3$ requires C, 73·35; H, 4·8; O, 9·2%). The crystals slowly darken in air; they are insoluble in water, ether, alcohol, benzene, and light petroleum but soluble in acetone and nitrobenzene [conductance in nitrobenzene ($1{\cdot}08 \times 10^{-3}$M), $\Lambda = 22{\cdot}8$ ohm^{-1} at 23°].

Method 2. The chloro-compound (0·509 g.) and sodium tetraphenylborate (0·903 g.) in acetone (3 ml.) were held at 25° under nitrogen for 6 days; the product gave yellow plates (0·157 g., 12·6%). The formation of the salt under these conditions must involve intermolecular transfer of carbon monoxide.

Chlorodicarbonyl-π-cyclopentadienyltriphenylphosphineiron Trihydrate.—Method 1. Chlorodicarbonyl-π-cyclopentadienyliron (1·3 g.) and triphenylphosphine (2·5 g.) in tetrahydrofuran (20 ml.) were heated under reflux until a vigorous reaction set in (*ca.* 5 min.) and a brown solid separated; heating was continued for a further 5 min. Filtration gave a brown amorphous powder which was extracted with hot water (2 × 10 ml.); the filtrate, on cooling, deposited yellow crystals. Repeated crystallisation from hot water and drying in a vacuum-desiccator gave a golden-yellow *trihydrate*, decomp. >120° (0·93 g., 30%) (Found: C, 56·7; H, 4·9; P, 5·8; Cl, 6·7; Fe, 10·4. $C_{35}H_{36}ClFeO_3P,3H_2O$ requires C, 56·8; H, 4·9; P, 5·9; Cl, 6·7; Fe, 10·6%). The salt is stable in air and readily soluble in hot but sparingly soluble in cold water. All the chloride is ionic and can be precipitated with silver ion. Addition of chloroplatinic acid to a solution gives a white precipitate of the *chloroplatinate* (Found: C, 46·2; H, 3·3; Cl, 16·6. $C_{50}H_{40}Cl_6Fe_2O_4P_2Pt$ requires C, 46·6; H, 3·1; Cl, 16·5%). Ammonium

[10] Green, Street, and Wilkinson, *Z. Naturforsch.*, 1959, **14**b, 738.
[11] Heck and Breslow, *J. Amer. Chem. Soc.*, 1960, **82**, 750, 4438.

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reineckate solution gave a pale pink *reineckate* which was crystallised from acetone–water (Found: C, 46·2; H, 3·6; N, 11·1. $C_{29}H_{36}CrFeN_6O_3P$ requires C, 46·0; H, 3·5; N, 11·1%). Bromine water gave a pale orange precipitate of the *tribromide*, which crystallised from chloroform (Found: C, 44·3; H, 3·2. $C_{25}H_{20}Br_3FeO_2P$ requires C, 44·2; H, 2·9%). In nitrobenzene at 23°, $0·83 \times 10^{-3}$M-π-$C_5H_5Fe(CO)_2PPh_3Cl,3H_2O$ had Λ 19·56 ohm^{-1}; $1·02 \times 10^{-3}$M-$[\pi\text{-}C_5H_5Fe(CO)_2PPh_3]_2PtCl_6$ had Λ 37·6 $ohm.^{-1}$.

Method 2. Equivalent amounts of the chloride reactant and triphenylphosphine were heated in a sealed tube.[7] Extraction of the product with benzene and chromatography on alumina gave tricarbonylbistriphenylphosphineiron, m. p. 272—275° (decomp.), in low yield. Extraction of the benzene-insoluble matter with hot water gave a yellow solution from which the cation was precipitated as the reineckate which crystallised as above (Found: C, 46·5; H, 3·6: N, 10·9%).

Triphenyl-arsine and -stibine Analogues.—The triphenylarsine and triphenylstibine cations could be prepared only by the sealed-tube method above. They were precipitated from their aqueous solutions as the *hexachloroplatinates* (Found: C, 43·2; H, 3·4; O, 5·1; Cl, 16·0. $C_{50}H_{40}As_2Cl_6Fe_2O_4Pt$ requires C, 43·6; H, 2·9; O, 4·7; Cl, 15·5%. Found: C, 41·0; H, 3·3; O, 5·3. $C_{50}H_{40}Cl_6Fe_2O_4PtSb_2$ requires C, 41·0; H, 2·8; O, 4·4%). They are less stable in air than the triphenylphosphine complex.

Dicarbonylcyclopentadienetriphenylphosphineiron.—Chlorodicarbonyl-π-cyclopentadienyltriphenylphosphine iron trihydrate (1·5 g.) was suspended in 2 : 1 tetrahydrofuran–ether (40 ml.) at *ca.* −10° under nitrogen and treated with small portions (*ca.* 0·25 g.) of sodium borohydride until the suspended salt was completely dissolved (*ca.* ½ hr.) and the solution was yellow. [This solution showed a weak high-field proton-resonance line identical with that of π-$C_5H_5Fe(CO)_2H$.] The solution was treated with air-free water (100 ml.) and extracted with light petroleum (b. p. 30—40°; 50 ml.). The petroleum layer [which rapidly darkened even under nitrogen owing to decomposition of π-$C_5H_5Fe(CO)_2H$] was washed with water, dried ($CaCl_2$), and concentrated to low bulk at 20°/2 mm. Chromatography on alumina (Brockmann, grade 3) under nitrogen gave a yellow weakly absorbed band which was rapidly eluted with ether and a dark red-brown strongly absorbed band from which, after extrusion, tetracarbonyldi-π-cyclopentadienyldi-iron was extracted with acetone (0·08 g., 7—8%; m. p. and mixed m. p. 193—194°). After removal of solvent from the yellow eluate at 20°/0·2 mm. a yellow solid (0·9 g., 75%) remained. Crystallisation from light petroleum (b. p. 30—40°) at −78° gave a golden-yellow *complex*, m. p. 113—114° (decomp.) (Found: C, 68·2; H, 4·8; P, 7·4; Fe, 12·4%; *M*, 420. $C_{25}H_{21}FeO_2P$ requires C, 68·25; H, 4·8; P, 7·05; Fe, 12·7%; *M*, 440). The compound decomposes within a few hours in air. On melting, it evolves a non-condensable gas and leaves a red oil. It is readily soluble in non-polar solvents, and the solutions darken over a period of days in absence of oxygen. Solutions in carbon disulphide begin to darken after 1 hr., whilst in carbon tetrachloride rapid decomposition (*ca.* 1 min.) occurs, producing chloroform and π-$C_5H_5Fe(CO)_2PPh_2Cl$, which was isolated as the chloroplatinate. The compound is moderately stable (*ca.* 1—2 days) in dichloromethane.

Thermal Decomposition of $C_5H_5Fe(CO)_2PPh_3$.—A solution of the compound (0·23 g.) in xylene (4—5 ml.) was heated under reflux for 5 min. After 1 min. the solution became deep red-brown. Chromatography with benzene eluate allowed the isolation of ferrocene, m. p. 171—173°; the compound $[\pi\text{-}C_5H_5Fe(CO)_2]_2$ (0·052 g., 60%), m. p. and mixed m. p. 189—192°, was recovered from the column by extraction with acetone.

Abstraction of Hydrogen from $C_5H_5Fe(CO)_2PPh_3$.—Triphenylmethyl tetrafluoroborate (0·15 g.) in dichloromethane (1—2 ml.) was added to a solution of the compound (0·123 g.) in dichloromethane (2 ml.). The reaction is only slow; after 12 hr. at *ca.* 5° the yellow crystals of *π-cyclopentadienyldicarbonyltriphenylphosphineiron tetrafluoroborate* were removed, washed with solvent and dried (0·102 g., 69%), decomp. >250° (Found: C, 56·0; H, 4·4. $C_{25}H_{20}BF_4FeO_2P$ requires C, 56·9; H, 3·8%).

Reduction of $[\pi\text{-}C_5H_5Fe(CO)_2][BPh_4]$.—A suspension of the salt (2·4 g.) in tetrahydrofuran (50 ml.) at −20° under nitrogen, on treatment with sodium borohydride, gave a deep yellow solution. This solution, which is similar in appearance to that obtained by reduction of π-$C_5H_5Fe(CO)_2Cl$ under the same conditions, shows a strong proton-resonance line at a position identical with that given by π-$C_5H_5Fe(CO)_2H$. Treatment of the solution with air-free water followed by extraction with light petroleum (b. p. 30—40°) caused rapid darkening of the organic layer. After removal of solvent at *ca.* 0°/0·1 mm., there remained purple crystals of

the compound $[\pi\text{-}C_5H_5Fe(CO)_2]_2$ (0·62 g., 75%), m. p. and mixed m. p. 194°; some of the readily volatile yellow complex $\pi\text{-}C_5H_5Fe(CO)_2H$ condensed in the cold trap during removal of solvent, and on melting decomposed with effervescence to give more of the binuclear product.

This experiment has been repeated several times and no evidence for a cyclopentadiene compound has been obtained.

Other Reactions of $\pi\text{-}C_5H_5Fe(CO)_2Cl$.—Refluxing this compound in tetrahydrofuran for 15 hr. under nitrogen afforded ferrocene and ferrous chloride; this reaction also occurs when the chloride is heated at 220°.[7] If equivalent amounts of phenyl- or diphenyl-acetylene are added, the products are the same. The addition of 2,2′-bipyridyl or 1,10-phenanthroline causes complete disruption, resulting in octahedral ferrous complexes such as chlorotris-1,10-phenanthrolineiron(II).

High-resolution Nuclear Magnetic Resonance Spectra.—Spectra were measured on a Varian model 43100 instrument at 56·43 Mc./sec. with 5-mm. (outside diameter) spinning sample tubes; tetramethylsilane was added as an internal reference and shifts are given in τ-values. $C_5H_6Fe(CO)_2PPh_3$ (in benzene and CS_2) gave 2·73, doublet (5·2 cycles/sec), phenyl protons; 4·87, " triplet " (4·2 cycles/sec.), H_3, H_4; 7·18, 7·38, H_β, 7·66, part of H_α; 7·79, H_2,H_5; 8·0, part of H_α.

Infrared Spectra.—The spectra in hexachlorobutadiene and Nujol mulls were taken on a Perkin–Elmer model 21 instrument with calcium fluoride and sodium chloride optics where appropriate. The assignments listed (in $cm.^{-1}$) are (a) C–H phenyl, (b) C–H olefin, (c) C–H_β, (d) C–H_α, (e) C_5H_5 out-of-plane deformation on PPh_3, (f) the same on BPh_4^-, (g) and (h) the same on $AsPh_3$ and $SbPh_3$, respectively, (i) O–H stretch, (j) O–H deformation, (k) C–O stretch, (l) BF_4^- asymmetric stretch, (m) spectra in CS_2 solution.

$C_5H_6Fe(CO)_2PPh_3$[m]: 3072w[a], 3010m[b], 2965w[c], 2765s[d], 1978vs[k], 1912vs[k], 1380vw, 1338vw, 1306vw, 1245vw, 1217w, 1186m, 1095m, 1073vw, 1055vw, 1030vw, 1000vw, 926vw, 830vw, 745s[e], 695s[e].

$[C_5H_5Fe(CO)_3][BPh_4]$: 3092vw, 3053vw; 2070vs[k], 2120vs[k]; 1580w, 1477m, 1433m, 1425m, 1305w, 1184w, 1153w, 1145w, 1115w, 1067w, 1033w, 1016vw, 1004w, 876w, 849w, 747s[f], 709s[f].

$[C_5H_5Fe(CO)_2PPh_3]Cl,3H_2O$: 3320vs[i]; 2030vs[k]; 2066vs[k]; 1635m[j], 1435m, 1308w, 1115w, 1095m, 1075vw, 998w, 875w, 745ms[e], 695s[e].

$[C_5H_5Fe(CO)_2PPh_3]_2PtCl_6$: 3080, 3100w; 2030vs[k], 2070s[k]; 1432m, 1310w, 1115w, 1096m, 1070vw, 998w, 875w, 750ms[e], 693ms[e].

$[C_5H_5Fe(CO)_2AsPh_3]_2PtCl_6$: 2017vs[k], 2062vs[k]; 1432m, 1303w, 1183vw, 1155vw, 1073vw, 1018vw, 998w, 865vw, 740vs[g], 690s[g].

$[C_5H_5Fe(CO)_2SbPh_3]_2PtCl_6$: 2005vs[k], 2050vs[k]; 1475m, 1435m, 1304vw, 1180vw, 1155vw, 1065vw, 1017vw, 997w, 874vw, 734ms[h], 690ms[h].

$[C_5H_5Fe(CO)_2PPh_3]BF_4$: 2033vs[k], 2069vs[k]; 1484m, 1438m, 1316w, 1288w, 1192w, 1172w, 1075vs[l], 873w, 750s[e], 695s[e].

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621. *Carbonate Derivatives of Methyl α-D-Mannopyranoside and of D-Mannose.*

By L. Hough and J. E. Priddle.

Reaction of methyl α-D-mannopyranoside (I) with an excess of benzyl chloroformate and aqueous sodium hydroxide gave methyl 4,6-di-*O*-benzyloxycarbonyl-α-D-mannopyranoside 2,3-carbonate (II; R = Ph·CH_2), which on catalytic hydrogenation yielded methyl α-D-mannopyranoside 2,3-carbonate (III). The latter was also prepared from methyl 4,6-*O*-benzylidene-α-D-mannopyranoside (IV) by the action of carbonyl chloride in toluene–pyridine and subsequent acid hydrolysis of the *O*-benzylidene group.

Reaction of D-mannose with benzyl chloroformate and aqueous sodium hydroxide afforded 1-*O*-benzyloxycarbonyl-α-D-mannofuranose 2,3:5,6-dicarbonate (VI).

Existing methods for the preparation and characterisation of carbohydrate carbonates have practical difficulties which severely limit the usefulness of these derivatives as suitably protected intermediates in synthesis.[1] Three general methods of esterification have been employed, namely, carbonyl chloride in an organic base,[2] a chloroformic ester in an organic base,[3] and a chloroformic ester in aqueous alkali.[4] The application of carbonyl chloride to carbonate preparations has been restricted by the poor yields obtained, frequently lower than 5%, and the obvious practical hazards involved. Of the two more convenient methods of synthesis using chloroformic esters, the reaction in organic base is less versatile since fully substituted *O*-alkyloxycarbonyl- and *O*-aryloxycarbonyl-derivatives are usually obtained,[1] whereas the reaction in aqueous alkali can give both cyclic and open-chain carbonates.[4] The stereochemical features of this reaction have been examined with reference to methyl α-D-mannopyranoside (I) [5] and D-mannose.

Investigation of the reaction conditions showed that above 5° the yield of product was seriously impaired,[6] presumably because of the comparatively rapid alkaline hydrolysis of both the chloroformic ester and the carbohydrate carbonate. However, when a mixture of either methyl chloroformate or ethyl chloroformate and an aqueous solution of methyl-α-D-mannopyranoside (I) was treated at 0° with aqueous sodium hydroxide, smooth reactions occurred to give the crystalline methyl di-*O*-alkyloxycarbonyl-α-D-mannopyranoside carbonates. On the other hand, the use of benzyl chloroformate in this reaction gave negligible product unless an equal volume of dioxan was added, whereupon a crystalline methyl di-*O*-benzyloxycarbonyl-α-D-mannopyranoside carbonate was produced in 60—90% yield. Clearly the conditions for these esterifications are critical and vary with the nature of the chloroformic ester.

In order to satisfy steric requirements,[5] the cyclic ester group in these three derivatives of methyl α-D-mannopyranoside (I) must be attached as a six-membered 4,6-carbonate or as a five-membered 2,3-carbonate. By analogy with the structures of the corresponding *O*-isopropylidene derivatives, the cyclic carbonates have generally been assumed to be five-membered although proof of this has seldom been attempted.[1] In this connection the C=O stretching frequency in the infrared spectrum can be used to distinguish between five- and six-membered carbonate rings,[7] and application of this technique to the mannopyranoside derivatives gave evidence that the cyclic carbonates were five-membered.[8]

[1] Hough, Priddle, and Theobald, *Adv. Carbohydrate Chem.*, 1960, **15**, 91.
[2] Haworth and Porter, *J.*, 1930, 151.
[3] Zemplén and László, *Ber.*, 1915, **48**, 915.
[4] Allpress and Haworth, *J.*, 1924, **125**, 1223.
[5] Hough and Priddle, *Chem. and Ind.*, 1959, 1600.
[6] Theobald, personal communication.
[7] Hough, Priddle, Theobald, Barker, Douglas, and Spoors, *Chem. and Ind.*, 1960, 148.
[8] Hough and Priddle, *J.*, 1961, 581.

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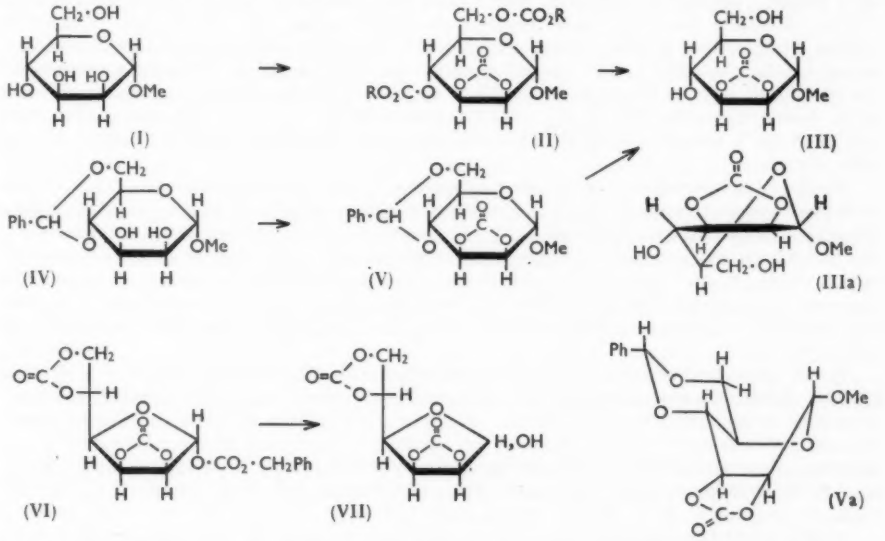
The *O*-benzyloxycarbonyl groups of the methyl di-*O*-benzyloxycarbonyl-α-D-mannopyranoside carbonate were selectively removed by catalytic hydrogenation,[9] using either Raney nickel or 10% palladium-on-charcoal as catalyst, with the formation of methyl α-D-mannopyranoside 2,3-carbonate (III). The latter was identified by comparison with an authentic specimen prepared from methyl 4,6-*O*-benzylidene-α-D-mannopyranoside (IV) by treatment with carbonyl chloride in the presence of pyridine, followed by acid hydrolysis of the 4,6-*O*-benzylidene residue in the resultant 2,3-carbonate (V). Thus, the structure of the product from the chloroformate reaction is firmly established as methyl 4,6-di-*O*-benzyloxycarbonyl-α-D-mannopyranoside 2,3-carbonate (II; R = $Ph{\cdot}CH_2$) and consequently the products from the reactions with methyl and ethyl chloroformate are assigned similar structures (II; R = Me and Et respectively). Fusion of the 2,3-carbonate ring



to the pyranoid chair conformation would be expected to bring $C_{(1)}$, $C_{(2)}$, $C_{(3)}$, and $C_{(4)}$ into co-planarity, and the cyclic carbonate derivative (III) would adopt a half-chair conformation (IIIa).[5] However, the *O*-benzylidene derivative (V) would tend towards a boat conformation (Va), as was suggested by molecular models and by the large difference in the molecular rotations of methyl 4,6-*O*-benzylidene-α-D-mannopyranoside (IV) ($[M]_D$ +17,900°) and its 2,3-carbonate ($[M]_D$ −5,850°).

In contrast to these pyranoside derivatives, the reaction of D-mannose with benzyl chloroformate in the presence of aqueous sodium hydroxide yielded a crystalline mono-*O*-benzyloxycarbonyl-D-mannose dicarbonate. Since catalytic hydrogenation of this compound gave the known D-mannofuranose 2,3:5,6-dicarbonate (VII),[2] the original product must be the 1-*O*-benzyloxycarbonyl derivative (VI). Comparison of the molecular rotation of the latter ($[M]_D$ +19,100°) with that of methyl α-D-mannofuranoside 2,3:5,6-dicarbonate ($[M]_{5780}$ +21,400°) [10] showed it to be the α-anomer.

Experimental

Unless otherwise stated, infrared spectra were obtained by the Nujol-mull technique. Optical rotations were measured at 24° ± 1°. M. p.s were determined on a Kofler micro-heating stage.

[9] Barker, Gillam, Lord, Douglas, and Spoors, *J.*, 1960, 3885.
[10] Haworth and Porter, *J.*, 1930, 649.

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Benzyl Chloroformate.—Benzyl chloroformate was obtained in 94% yield by the dropwise addition of benzyl alcohol to excess of liquid carbonyl chloride cooled in a bath of ethanol–solid carbon dioxide. Hydrogen chloride and excess of carbonyl chloride were removed by drawing a current of dry air through the liquid. Benzyl chloroformate was characterised as its carbamate derivative.[11]

Methyl 4,6-*Di*-O-*benzyloxycarbonyl*-α-D-*mannopyranoside* 2,3-*Carbonate* (II; R = CH_2Ph).—Methyl α-D-mannopyranoside (19·4 g.) was dissolved in water (50 ml.), and to the solution was added benzyl chloroformate (100 ml., 6 mol.) previously neutralised by the addition of a little sodium hydrogen carbonate. Dioxan (100 ml.) was added and the reaction mixture was vigorously stirred at 0° whilst 3N-sodium hydroxide (200 ml.) was added dropwise during about 3 hr. Stirring was continued until the pH had fallen to a constant value. Water was then added to dissolve any precipitated sodium salts, the solution was extracted with chloroform (3 × 200 ml.), and the extracts dried ($CaSO_4$) and concentrated under reduced pressure to a thin syrup. Aromatic impurities were removed in a high vacuum at 170° (bath). The brown residue was dissolved in ethanol (charcoal) and filtered, and the clear solution concentrated to a syrup which crystallised after several months (60—90% yield in different preparations). Recrystallisation from ethanol gave *methyl* 4,6-*di*-O-*benzyloxycarbonyl*-α-D-*mannopyranoside* 2,3-*carbonate*, m. p. 111—111·5°, $[\alpha]_D$ +10·7° (*c* 1·1 in $CHCl_3$); $\nu_{max.}$ (C=O stretching) 1740, 1750, and 1830 cm.$^{-1}$ (Found: C, 59·0; H, 4·8; OMe, 6·9. $C_{24}H_{24}O_{11}$ requires C, 59·0; H, 4·9; OMe, 6·4%).

Methyl 4,6-*Di*-O-*methoxycarbonyl*-α-D-*mannopyranoside* 2,3-*Carbonate* (II; R = Me).—Methyl α-D-mannopyranoside (5 g.), in a mixture of methyl chloroformate (37 g.) and chloroform (50 ml.), was treated as above with 7·5% (w/v) sodium hydroxide (200 ml.). Evaporation of the chloroform extract gave a sticky solid (5 g.) which crystallised from chloroform–light petroleum (b. p. 40—60°) to give *methyl* 4,6-*di*-O-*methoxycarbonyl*-α-D-*mannopyranoside* 2,3-*carbonate* (2 g.), m. p. 172°, $[\alpha]_D$ +23·6° (*c* 1·1 in $CHCl_3$), and $\nu_{max.}$ (C=O stretching) 1745, 1755, and 1830 cm.$^{-1}$ (Found: C, 42·6; H, 5·0; OMe, 27·7. $C_{12}H_{16}O_{11}$ requires C, 42·8; H, 4·8; OMe, 27·7%).

Methyl 4,6-*Di*-O-*ethoxycarbonyl*-α-D-*mannopyranoside* 2,3-*Carbonate* (II; R = Et).—A mixture of methyl α-D-mannopyranoside (5 g.) and ethyl chloroformate (27 g.) was treated with 3N-sodium hydroxide (100 ml.) as above. *Methyl* 4,6-*di*-O-*ethoxycarbonyl*-α-D-*mannopyranoside* 2,3-*carbonate* was obtained as a yellow syrup (*ca.* 90% yield) which gave crystals after several months. Recrystallised from ethanol they had m. p. 117—117·5°, $[\alpha]_D$ +15·5° (*c* 1·1 in $CHCl_3$), $\nu_{max.}$ (C=O stretching) 1740, 1752, and 1832 cm.$^{-1}$ (Found: C, 45·8; H, 5·5; OAlk, 32·7. $C_{14}H_{20}O_{11}$ requires C, 46·1; H, 5·5; OAlk, 33·2%).

Methyl 4,6-O-*Benzylidene*-α-D-*mannopyranoside* 2,3-*Carbonate* (V).—A solution of carbonyl chloride (1 g.) in toluene (11·4 g.) was added dropwise to a stirred solution of methyl 4,6-*O*-benzylidene-α-D-mannopyranoside [12] (1 g.) in a mixture of pyridine (5 ml.) and chloroform (10 ml.), cooled in an ice-bath. After being stirred overnight, the brown solution was carefully treated with water (10 ml.), and more chloroform (25 ml.) was added. The chloroform layer was separated, dried ($CaSO_4$), and evaporated to a yellow syrup which on trituration with acetone–ether gave crystals of *methyl* 4,6-O-*benzylidene*-α-D-*mannopyranoside* 2,3-*carbonate* (1 g.). After decolorisation with activated charcoal, and recrystallisation from acetone, the crystals had m. p. 125°, $[\alpha]_D$ −19·0° (*c* 1·2 in $CHCl_3$), and $\nu_{max.}$ (C=O stretching) 1810 cm.$^{-1}$ (Found: C, 58·1; H, 5·4. $C_{15}H_{16}O_7$ requires C, 58·4; H, 5·2%).

Methyl α-D-*Mannopyranoside* 2,3-*Carbonate* (III).—(*a*) Methyl 4,6-di-*O*-benzyloxycarbonyl-α-D-mannopyranoside 2,3-carbonate (2·2 g.) was dissolved in dioxan (100 ml.), and 10% palladium–charcoal (1 g.) added. The mixture was hydrogenated at atmospheric pressure at 20° until hydrogen consumption ceased. After filtration, the solution was dried ($CaSO_4$) and evaporated to give crystals of *methyl* α-D-*mannopyranoside* 2,3-*carbonate* (1 g.). Recrystallised from acetone–ether they had m. p. 157—158°, $[\alpha]_D$ +56·9° (*c* 1·0 in $CHCl_3$), and $\nu_{max.}$ (C=O stretching) 1810 cm.$^{-1}$ (Found: C, 43·7; H, 5·7; OMe, 14·5. $C_8H_{12}O_7$ requires C, 43·7; H, 5·5; OMe, 14·1%).

(*b*) A solution of methyl 4,6-*O*-benzylidene-α-D-mannopyranoside 2,3-carbonate (0·35 g.) in a mixture of acetone (8 ml.) and N-hydrochloric acid (2 ml.) was kept at room temperature for 24 hr., neutralised (Ag_2CO_3), filtered, and then evaporated to dryness under reduced pressure.

[11] Carter, Frank, and Johnson, *Org. Synth.*, 1943, **23**, 13.
[12] Schwarz, unpublished method.

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The residue was extracted with boiling ether, leaving crystals of methyl α-D-mannopyranoside 2,3-carbonate (0·21 g.) which had $[\alpha]_D$ +58° (*c* 1·0 in $CHCl_3$), m. p. 158° unchanged on admixture with the sample obtained by method (*a*), and an infrared spectrum identical with the above (Found: C, 43·5; H, 5·7; OMe, 14·7%).

1-O-*Benzyloxycarbonyl*-α-D-*mannofuranose* 2,3:5,6-*Dicarbonate* (VI).—To D-mannose (9 g.) in water (20 ml.) was added sodium hydrogen carbonate (1 g.) and a solution of benzyl chloroformate (50 ml.) in dioxan (50 ml.). The mixture was cooled to 0° and 3N-sodium hydroxide (100 ml.) was added dropwise with continuous stirring. After being stirred overnight the mixture was treated with chloroform, and a sticky solid separated from the organic layer. After trituration with more chloroform, crystals of 1-O-*benzyloxycarbonyl*-α-D-*mannofuranose* 2,3:5,6-*dicarbonate* (7·8 g.) were obtained which, after recrystallisation from acetone–light petroleum (b. p. 60—80°), had m. p. 168—169·5°, $[\alpha]_D$ +52·1° (*c* 1·6 in Me_2CO), and $\nu_{max.}$ (C=O stretching) 1765, 1801, and 1845 cm.$^{-1}$ (Found: C, 52·4; H, 4·0. $C_{16}H_{14}O_{10}$ requires C, 52·4; H, 3·8%).

D-*Mannofuranose* 2,3:5,6-*Dicarbonate* (VII).—(*a*) A solution of 1-*O*-benzyloxycarbonyl-α-D-mannofuranose 2,3:5,6-dicarbonate (5 g.) in dioxan (100 ml.) was hydrogenated at 20° and atmospheric pressure, 10% palladium–charcoal (1 g.) being used as catalyst. After filtration, evaporation to dryness gave crystals of D-mannofuranose 2,3:5,6-dicarbonate (2·8 g.) which on recrystallisation from water and then from ethanol–light petroleum (b. p. 60—80°) had m. p. 119—120°, $[\alpha]_D$ +30·2° (*c* 1·4 in Me_2CO) and $\nu_{max.}$ (C=O stretching) 1770, 1800, and 1830 cm.$^{-1}$ (Found: C, 41·5; H, 3·2. Calc. for $C_8H_8O_8$: C, 41·4; H, 3·4%). Only two C=O stretching absorptions with $\nu_{max.}$ 1800 and 1820 cm.$^{-1}$ were observed (KBr disc).

(*b*) By the method of Haworth and Porter,[2] D-mannose (6 g.) was dissolved in pyridine (40 ml.), cooled to 0° and treated with a stream of carbonyl chloride for 40 min. After the addition of ice–water (200 ml.) the insoluble amorphous material (4·2 g.) was discarded and the filtrate treated with excess of barium carbonate, filtered, and extracted with ethyl acetate (3 × 200 ml.). On evaporation of the extracts a yellow syrup (1 g.) was obtained which, after trituration with ethyl methyl ketone, yielded crystals of D-mannofuranose 2,3:5,6-dicarbonate (0·25 g.). Recrystallised from ethanol–light petroleum (b. p. 60—80°) they had m. p. and mixed m. p. 119—120°, $[\alpha]_D$ +29·4° (*c* 1·3 in Me_2CO), and identical infrared spectrum with the above (Found: C, 41·4; H, 3·5%).

We thank Dr. J. C. P. Schwarz for a sample of methyl 4,6-*O*-benzylidene-α-D-mannopyranoside, Dr. R. S. Theobald for his interest and advice, and the Department of Scientific and Industrial Research for a grant to J. E. P.

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622. *Studies in Stereochemical Structure. Part XIV.*[1] *The Resolution of α-Hydroxy-amidinium Chlorides by the Use of Mandelic Acids.*

By ROBERT ROGER and DOUGLAS G. NEILSON.

(±)-α-Hydroxy-α- and -β-phenylbutyramidinium chlorides have been synthesised and have been resolved by use of mandelic acids. The specific rotation of (+)-α-hydroxy-α-phenylbutyric acid prepared from the (+)-α-hydroxy-α-phenylbutyramidinium chloride showed the latter to be almost optically pure. In the case of the β-phenylamidinium chloride, although resolution was established, the extent could not be determined owing to lack of reference data.

THE readily accessible, optically active mandelic acids[2] are useful agents for the resolution of various types of (±)-bases. They have the advantages of sharp melting points (133°) and high specific rotations, $[\alpha]_{5461}$ ±190° (in acetone). In addition, they are soluble in the

[1] Part XIII, *J.*, 1960, 627.
[2] Roger, *J.*, 1935, 1544.

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more usual organic solvents and their sodium or ammonium salts [3] are readily available for the resolution of (±)-base hydrochlorides or sulphates. Typical examples of their use are the preparation of (−)-ephedrine [4,5] and related compounds of the ephedrine series,[6] amines,[7,8,9] amino-glycols,[10,11] R·CH(OH)·CH(NH_2)·CH_2·OH (R = *p*-NO_2·C_6H_4 and *p*-Me·SO_2·C_6H_4), and s-butylmercury compounds.[12] We have also used them to prepare (−)-mandelamidinium chloride [1,13] and the (+)- and (−)-atrolactamidinium chloride.[14]

We have now prepared (±)-α-hydroxy-α- and -β-phenylbutyramidinium chloride and resolved them in a similar way. Pure propiophenone cyanohydrin, obtained by distillation *in vacuo* in the presence of iodine [15] as stabiliser, was converted by the Pinner synthesis [16,17] into ethyl (±)-α-hydroxy-α-phenylbutyrimidate hydrochloride (I) which on treatment with alcoholic ammonia yielded (±)-α-hydroxy-α-phenylbutyramidinium chloride (II). This furnished a (±)-mandelate on treatment with aqueous sodium (±)-mandelate.

The (±)-amidinium chloride and sodium (−)-mandelate in water deposited (+)-α-hydroxy-α-phenyl-butyramidinium (−)-mandelate which was optically pure after three crystallisations and with hydrogen chloride gave (+)-α-hydroxy-α-phenylbutyramidinium chloride, $[\alpha]_{5461}$ +48·9° (in water). The mother-liquors from the (+)-base (−)-acid salt, when treated with hydrochloric acid and freed from mandelic acid, deposited (−)-α-hydroxy-α-phenyl-butyramidinium chloride, having $[\alpha]_{5461}$ −48·9° (in water), but with a melting point below that of its enantiomorph. Crystallisation did not improve its melting point substantially, but purification through its (+)-mandelate gave a chloride that agreed in melting point and rotatory power with its enantiomorph.

(I) (±)-HO·CPhEt·C(OEt):NH_2Cl ⟶ (±)-HO·CPhEt·C(NH_2):NH_2Cl (II)

With hot aqueous sodium hydroxide, (+)-α-hydroxy-α-phenylbutyramidinium chloride, $[\alpha]_{5461}$ +47·8° (in water; *i.e.*, 97% of the previous value), gave (+)-α-hydroxy-α-phenylbutyric acid, $[\alpha]_{5461}$ +37·0° (in water). This value represents 97% of the specific rotation, $[\alpha]_{5461}$ −38·1° (in water), found by McKenzie and Ritchie,[18] and hence the resolution is regarded as almost complete. Moreover, as this hydrolysis occurs in a position remote from the asymmetric centre, the (+)-amidinium chloride and (+)-α-hydroxy-α-phenylbutyric acid will be related in absolute configuration.

Attempts to form the (±)-, (+)-, and (−)-α-hydroxy-α-phenylbutyramidines from their respective hydrochlorides by the action of sodium hydroxide solutions of varying strengths failed. Somewhat similar difficulties were encountered by Reid [19] who obtained (±)-mandelamidine but not (+)- or (−)-mandelamidine and by Roger and Neilson [14] who failed to isolate (+)- and (−)-atrolactamidine.

The isomeric (±)-α-hydroxy-β-phenylbutyramidinium chloride with sodium (±)-mandelate gave a monohydrated (±)-amidinium (±)-mandelate that became anhydrous *in vacuo* at 100°: in one instance, under apparently identical conditions, a non-hydrated

[3] McKenzie and Walker, *J.*, 1928, 646.
[4] Manske and Johnson, *J. Amer. Chem. Soc.*, 1929, **51**, 1906.
[5] Skita, Keil, and Meiner, *Ber.*, 1933, **66**, 974.
[6] Jarowski and Hartung, *J. Org. Chem.*, 1943, **8**, 564.
[7] Ingersoll and DeWitt, *J. Amer. Chem. Soc.*, 1951, **73**, 3360.
[8] Brode and Raasch, *J. Amer. Chem. Soc.*, 1942, **64**, 1449.
[9] Roger, unpublished work.
[10] Crooks, jun., Rebstock, Controulis, and Bartz, U.S.P., 2,483,884.
[11] Rebstock and Bambas, *J. Amer. Chem. Soc.*, 1955, **77**, 186.
[12] Jensen, Whipple, Wedegaetner, and Landgrebe, *J. Amer. Chem. Soc.*, 1959, **81**, 1262.
[13] Neilson, Ph.D. Thesis, St. Andrews, 1955.
[14] Roger and Neilson, *J.*, 1959, 688.
[15] Hansley, U.S.P. 2,416,624.
[16] Roger and Neilson, *Chem. Rev.*, 1961, **61**, 179.
[17] Pinner, " Die Imidoäther und ihre Derivate," Oppenheim, Berlin, 1892.
[18] McKenzie and Ritchie, *Ber.*, 1937, **70**, 23.
[19] Reid, Ph.D. Thesis, St. Andrews, 1949.

form of the (±)-mandelate was obtained, despite the reaction's taking place in water. Whilst hydration of amidinium salts is not very usual, Ashley and his co-workers [20] report several cases.

Use of sodium (−)-mandelate produced, after four crystallisations, (−)-α-hydroxy-β-phenylbutyramidinium (−)-mandelate hemihydrate which yielded a lævorotatory chloride on treatment with hydrogen chloride. Decomposition of the mother-liquors from the (−) (−)-salt with hydrochloric acid yielded inactive chloride, showing that the separation of the diastereoisomers took place mainly during the subsequent recrystallisations, and hence the final yields were small. The diastereoisomeric (+)-α-hydroxy-β-phenylbutyramidinium (+)-mandelate hemihydrate was obtained in a similar way by using sodium (+)-mandelate. Decomposition of the (−)-amidinium chloride with hot alkali furnished a (−)-α-hydroxy-β-phenylbutyric acid, but we have found no recorded rotations for this acid or its diastereoisomers and therefore cannot estimate the extent of resolution. Moreover, paucity of the final amidinium mandelate samples precluded the determination of optical purity by crystallisation to constant rotatory power.

Experimental

Specific rotations were measured in a 2-dm. tube unless otherwise stated.

Optically Active Mandelic Acids.—These acids [2] and the calculated quantity of sodium hydrogen carbonate solution were evaporated and the residues of sodium salts were recrystallised from aqueous ethanol.

Propiophenone Cyanohydrin.—Propiophenone (134 g.) in ether (100 ml.) was added to a solution of sodium cyanide (123 g.) in water (150 ml.). The mixture was stirred at 5° during addition of concentrated hydrochloric acid (210 ml.). The addition required 2 hr. and the mixture was then stirred for a further hr. at 5°, then extracted with ether. The extract, after drying (Na_2SO_4), afforded propiophenone cyanohydrin (54 g.), b. p. 148—150°/16 mm. in the presence of iodine (0·5 g.) as stabiliser.[15]

Hydratropaldehyde Cyanohydrin.[21]—Freshly distilled hydratropaldehyde (36 g.) was stirred with a solution of sodium cyanide (12·5 g.) in water (50 ml.) and ice (100 g.). Saturated sodium hydrogen sulphite solution (72 ml.) was run slowly into the stirred mixture. Stirring was continued for ½ hr., then the solution was extracted with ether. The ether was removed from the dried extract (Na_2SO_4), and the cyanohydrin again dried (Na_2SO_4) and then converted directly into the imidate hydrochloride.

Imidate Hydrochlorides.—These were prepared by the Pinner method,[16,17] interaction of equimolar quantities of the cyanohydrin, ethanol, and hydrogen chloride under anhydrous conditions. After 24 hr. at 0° the reactants were treated with anhydrous ether. The imidate salts crystallised almost immediately.

Ethyl (±)-α-hydroxy-α-phenylbutyrimidate hydrochloride (45%) had m. p. 98—99° (decomp.). The hydrochloride (4·8 g.) with 4N-sodium hydroxide (12 ml.) yielded the *imidate* (3·4 g.), m. p. 71—72° [from light petroleum (b. p. 60—80°)] (Found: C, 69·9; H, 8·3; N, 6·9. $C_{12}H_{17}NO_2$ requires C, 69·6; H, 8·2; N, 6·8%).

Ethyl (±)-α-hydroxy-β-phenylbutyrimidate hydrochloride (60%) had m. p. 108—109°.

Amidinium Chlorides.—The imidate hydrochlorides (0·1 mole) were shaken with anhydrous solutions of ammonia (8·5 g.) in ethanol (100 ml.) for 8 hr. and the alcohol then evaporated at room temperature. The resultant amidinium chlorides were recrystallised from dilute hydrochloric acid [samples for analysis were prepared by decomposition of the (±)-mandelate salts with hydrogen chloride].

(±)-α-*Hydroxy-α-phenylbutyramidinium chloride* (72%) had m. p. 133—134° (decomp.) (Found: C, 55·5; H, 7·1; N, 13·2. $C_{10}H_{15}ClN_2O$ requires C, 55·9; H, 7·0; N, 13·05%).

(±)-α-*Hydroxy-β-phenylbutyramidinium chloride* (80%) contracted at 250° and melted at 259—260° (decomp.) after darkening (Found: C, 56·25; H, 7·0; N, 13·1%).

(±)-*Amidinium* (±)-*Mandelates.*—Equimolar quantities of sodium (±)-mandelate and

[20] Ashley, Barber, Ewins, Newbery, and Self, *J.*, 1942, 103.
[21] Biquard, *Compt. rend.*, 1932, **194**, 983.

amidinium chloride were heated together in water until a clear solution resulted. The crystals which separated on cooling were twice recrystallised from water (charcoal). (±)-α-*Hydroxy*-α-*phenylbutyramidinium* (±)-*mandelate* (52%) softened at 171° and melted at 173—174° (decomp.) (Found: C, 65·4; H, 6·4; N, 8·55. $C_{18}H_{22}N_2O_4$ requires C, 65·5; H, 6·7; N, 8·5%).

(±)-α-*Hydroxy*-β-*phenylbutyramidinium* (±)-*mandelate monohydrate* (53%), after drying *in vacuo* below 50°, contracted at 76° and melted at 82—83° (Found: C, 62·0; H, 6·9; N, 8·4. $C_{18}H_{22}N_2O_4,H_2O$ requires C, 62·1; H, 6·9; N, 8·05%). In one instance a similar preparation resulted in an anhydrous *salt* which softened at 160° and melted at 165—166° (decomp.) (Found: C, 65·3; H, 6·5; N, 8·4%). A mixed m. p. with the hydrate was at 154—155°. The monohydrate, on drying *in vacuo* at 100° to constant weight (5 hr.) lost 17·9 parts by weight per mole.

Optically Active Amidinium Mandelates.—(a) α-*Hydroxy*-α-*phenylbutyramidinium salts.* (±) α-Hydroxy-α-phenylbutyramidinium chloride (5·4 g.) and sodium (−)-mandelate (4·4 g.), $[\alpha]_{5461}$ −120° (in water), were heated in water (50 ml.). The solid which was deposited on cooling was recrystallised three times from water, giving rhombic crystals of (+)-α-*hydroxy*-α-*phenylbutyramidinium* (−)-*mandelate* (1·2 g.), which softened at 172° and had m. p. 175—176° (decomp), $[\alpha]^{17}_{5461}$ −9·9° (*c* 0·96 in methanol) (Found: C, 66·15; H, 6·7; N, 8·3%).

(−)-α-*Hydroxy*-α-*phenylbutyramidinium* (+)-*mandelate*, prepared as above from sodium (+)-mandelate, $[\alpha]_{5461}$ +120° (in water), softened at 172°, and had m. p. 175—176° (decomp.), $[\alpha]^{17}_{5461}$ +9·3° (*c* 0·78 in methanol) (Found: C, 65·2; H, 6·4; N, 8·55%).

(b) α-*Hydroxy*-β-*phenylbutyramidinium salts.* (±)-α-Hydroxy-β-phenylbutyramidinium chloride (10·7 g.) and sodium (−)-mandelate, $[\alpha]_{5461}$ −121° (in water), in water (125 ml.) gave rhombic crystals that were recrystallised thrice from water, giving (−)-α-*hydroxy*-β-*phenylbutyramidinium* (−)-*mandelate hemihydrate* (1·5 g.) as needles which softened at 115°, became yellow at 160°, and melted at 174—175° (decomp.), and had $[\alpha]^{18}_{5461}$ −102·3° (*c* 0·98 in methanol) (Found: C, 63·5; H, 6·8; N, 8·25. $C_{18}H_{22}N_2O_4,\frac{1}{2}H_2O$ requires C, 63·7; H, 6·8; N, 8·3%).

(+)-α-*Hydroxy*-β-*phenylbutyramidinium* (+)-*mandelate hemihydrate* was prepared similarly from sodium (+)-mandelate, $[\alpha]_{5461}$ +120° (in water), and had m. p. 174—175° (decomp.), after softening at 115° and becoming yellow at 160°, $[\alpha]^{17}_{5461}$ +105·8° (*c* 0·58 in methanol) (Found: C, 63·3; H, 6·7; N, 8·15%). Solid which was deposited after the original reaction liquors had been decomposed with hydrochloric acid and the liberated mandelic acid removed with ether proved to be (±)-α-hydroxy-β-phenylbutyramidinium chloride.

Optically Active Amidinium Chlorides.—A cooled solution of the optically active amidinium mandelate in alcohol was treated with dry hydrogen chloride and set aside for 24 hr. The alcohol was then evaporated *in vacuo* and the resultant solid treated several times with hot benzene–acetone to remove mandelic acid. The residue was then washed with ether, dissolved in warm alcohol, cooled, and reprecipitated with ether. The yields were almost theoretical.

(+)-α-*Hydroxy*-α-*phenylbutyramidinium chloride*, prepared from (+ −)-salt of $[\alpha]_{5461}$ −9·9°, melted at 201—202° (decomp.) and had $[\alpha]^{19}_{5461}$ +48·9° (*c* 0·44 in water) (Found: C, 55·9; H, 6·9; N, 13·2. $C_{10}H_{15}ClN_2O$ requires C, 55·9; H, 7·0; N, 13·05%).

(1) (−)-α-*Hydroxy*-α-*phenylbutyramidinium chloride*, prepared from (− +)-salt of $[\alpha]_{5461}$ +9·3°, had m. p. 201—202° (decomp.) and $[\alpha]^{17}_{5461}$ −49° (*c* 0·68 in water) (Found: C, 55·7; H, 7·0; N, 13·2%).

The mother-liquors from the (+)-salt were heated with hydrochloric acid and the mandelic acid liberated was removed with ether. After 2 days the solution deposited (−)-α-hydroxy-α-phenylbutyramidinium chloride, $[\alpha]^{17}_{5461}$ −48·9°, m. p. 179—180°.

(−)-α-*Hydroxy*-β-*phenylbutyramidinium chloride*, from (− −)-salt of $[\alpha]_{5461}$ −102·3°, softened at 197°, melted at 210—212°, and decomposed above 215° and had $[\alpha]^{13}_{5461}$ −43·6° (*c* 0·86 in water) (Found: C, 55·7; H, 6·75; N, 13·0%).

(+)-α-*Hydroxy*-α-*phenylbutyric Acid.*—(+)-α-Hydroxy-α-phenylbutyramidinium chloride (0·4 g.), $[\alpha]^{30}_{5461}$ +47·8° (in water), was heated in 4N-sodium hydroxide (5 ml.) until evolution of ammonia ceased. The acidified solution, on extraction with ether, evaporation of this extract, and crystallisation of the resultant solid from benzene (charcoal), yielded (+)-α-hydroxy-α-phenylbutyric acid (0·1 g.), $[\alpha]^{22}_{5461}$ +37° (*c* 0·27 in water). A mixed m. p. with authentic (+)-acid was satisfactory.

(−)-α-*Hydroxy*-β-*phenylbutyric Acid.*—(−)-α-Hydroxy-β-phenylbutyramidinium chloride (0·3 g.), $[\alpha]_{5461}$ −43·6° (in water), treated as above, gave (−)-α-hydroxy-β-phenylbutyric acid which softened at 123°, melted at 130—131°, and had $[\alpha]^{18}_{5461}$ −24·0° (*c* 0·19 in water). The smallness of the sample precluded analysis.

One of us (D. G. N.), now an Edward A. Deeds Research Fellow, of Queen's College, Dundee, is indebted to the University of St. Andrews for a Post Graduate Scholarship which enabled part of the foregoing work to be undertaken.

QUEEN'S COLLEGE, DUNDEE,
UNIVERSITY OF ST. ANDREWS. [*Received, February 23rd,* 1961.]

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623. *The Reaction of Cyanogen Chloride with Sodium Salts of Carboxylic Acids.*

By J. A. BARLTROP, A. C. DAY, and (in part) D. B. BIGLEY.

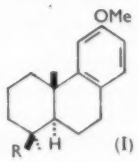
With cyanogen chloride at 250°, the sodium salts of an axial and an equatorial carboxylic acid give nitriles, with retention of configuration.

IT has been shown [1] that nitriles can be obtained in good yield by the reaction between cyanogen chloride and alkali-metal salts of numerous carboxylic acids at 200—300°. For the corresponding reactions of cyanogen bromide, tracer studies [2,3] have given results in accordance with the scheme:

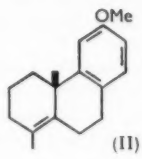
$$R{\cdot}{}^{*}CO_2Na + Br{\cdot}CN \xrightarrow{250-300^\circ} R{\cdot}{}^{*}CN + CO_2 + NaBr \quad (R = Et, Ph)$$

i.e., the carbon atom liberated as carbon dioxide is derived from the cyanogen halide, and the bond between alkyl radical R and the carboxyl carbon atom is not broken. A minor product is an α-keto-isocyanate (R·CO·NCO), and a mechanism involving this compound as intermediate has been suggested.[3] We present here stereochemical evidence as to the course of the reaction.

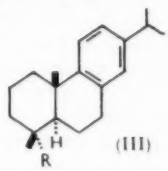
Sodium *O*-methylpodocarpate (I; R = CO_2Na), when heated in a sealed tube at 250° with cyanogen chloride, gave a 26% yield of the corresponding nitrile (I; R = CN), identical with a sample which we prepared by an unambiguous method (cf. ref. 4). Although searched for meticulously, the nitrile with inverted stereochemistry at position 1 (phenanthrene numbering) was not detected. A second product, $C_{17}H_{22}O$, b. p. 115°/0·1 mm., was probably the $\Delta^{1(11)}$-olefin (II), since the ethylenic bond was not revealed in the infrared spectrum. A very small quantity of carbonyl-containing material, ν 1742 and 1721 cm.$^{-1}$, could not be obtained free from nitrile, and so remains uncharacterized.



(I)



(II)



(III)

Under the same conditions, sodium dehydroabietate (III; R = CO_2Na) gave the known dehydroabietonitrile (III; R = CN) (32%) and none of its $C_{(1)}$-epimer. The by-products of this reaction appeared to be similar to those obtained from sodium *O*-methylpodocarpate.

The retention of configuration in both the equatorial (III; R = CO_2Na) and the axial (I; R = CO_2Na) carboxylate is consistent with the suggested mechanism,[3] and not with any simple mechanism involving replacement at the α-carbon atom.

[1] Zappi and Bouso, *Anales Asoc. quím. Argentina*, 1947, **35**, 137 (*Chem. Abs.*, 1948, **42**, 7704); cf. Cahours, *Annalen*, 1858, **108**, 319; Cloëz, *ibid.*, 1860, **115**, 23.
[2] Douglas, Eccles, and Almond, *Canad. J. Chem.*, 1953, **31**, 1127.
[3] Douglas and Burditt, *Canad. J. Chem.*, 1958, **36**, 1256.
[4] Wenkert and Jackson, *J. Amer. Chem. Soc.*, 1958, **80**, 211.

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Experimental

M. p.s were determined on a Kofler block. Infrared spectra were determined for liquid films unless otherwise stated. Optical rotations are for chloroform solutions. For chromatography, Peter Spence's " Grade H " alumina was used; deactivated alumina contained 5% of 10% aqueous acetic acid. Unless otherwise stated, light petroleum refers to the fraction of b. p. 60—80°.

O-*Methylpodocarponitrile* (I; R = CN).—*O*-Methylpodocarpoyl chloride (I; R = COCl) [5] (1·01 g.) in dry tetrahydrofuran (35 ml.) was stirred with a suspension of sodamide (from 3·5 g. of sodium) in liquid ammonia (250 ml.) until most of the ammonia had evaporated (*ca.* 8 hr.). The oily product (0·96 g.) was isolated with chloroform and chromatographed on alumina (50 g.). Elution with 1 : 1 light petroleum–benzene (600 ml.) followed by recrystallization from light petroleum gave O-*methylpodocarponitrile* (I; R = CN) (107 mg.) as needles, m. p. 106—108·5°. Recrystallized again, it had m. p. 108—109°, $[\alpha]_D^{16}$ +58·1° (*c* 1·09) (Found: C, 80·3; H, 8·8; N, 5·2. $C_{18}H_{23}NO$ requires C, 80·3; H, 8·6; N, 5·2%). Elution with methanol (200 ml.) and crystallization from ether gave a solid (250 mg.) from which O-*methylpodocarpamide* (I; R = CO·NH_2) (160 mg.), m. p. 157—159°, was obtained on recrystallization from methanol. The analytical sample, recrystallized once more from methanol, had m. p. 160°, $[\alpha]_D^{16}$ +149° (*c* 1·33) (Found: C, 75·3; H, 9·1; N, 4·7. $C_{18}H_{25}NO_2$ requires C, 75·3; H, 8·7; N, 4·9%).

Cyanogen Chloride Reactions.—Cyanogen chloride was prepared from chlorine and sodium cyanide,[6] and was stored in sealed ampoules each containing 0·5—1 g.

(*A*) *O*-Methylpodocarpic acid [7] (0·62 g.) in ethanol was treated with the calculated quantity of sodium ethoxide in ethanol. Removal of the solvent *in vacuo* and recrystallization from water gave the sodium salt (I; R = CO_2Na) (0·56 g.) as needles, which were dried at 175°/0·1 mm.

The sodium salt (430 mg.) was sealed in a Carius tube at −60° with the contents of one ampoule of cyanogen chloride. After being shaken vigorously at room temperature, the tube was heated at 250° for ¾ hr., with occasional shaking. The tube was opened at −60°, and the excess of cyanogen chloride was removed under reduced pressure. After the addition of water, the oily neutral product (290 mg.) was isolated with ether. (No acidic material was obtained on acidification of the aqueous layer combined with the alkali washings of the ethereal solution.) Chromatography on deactivated alumina (60 g.) and elution with 4 : 1 light petroleum–benzene (120 ml.) gave an oil (56 mg.) which, after distillation, had b. p. 115° (bath)/0·1 mm., ν 1212m, 1170m, 1066w, 871m, 835m, and 800 $cm.^{-1}$ (no bands due to C⋮N or C⋮O) (Found: C, 83·2, 83·4; H, 8·7, 8·9. $C_{17}H_{22}O$ requires C, 84·3; H, 9·2%). Further elution with the same solvent mixture (60 ml.) gave a semisolid fraction (29 mg.), ν 2227 (C⋮N), 1742, and 1721 $cm.^{-1}$ (C⋮O); and then (with 240 ml. of solvent) *O*-methylpodocarponitrile (I; R = CN) (89 mg.), m. p. 98—103°. Elution with benzene and finally with ether gave intractable resins (52 mg.) which were not investigated further. Rechromatography of the semisolid fraction gave a mixed fraction (16 mg.) and the nitrile (7 mg.).

After recrystallization from light petroleum (b. p. 40—60°), the nitrile was obtained as needles, m. p. 107—108° (undepressed by admixture with an authentic sample), $[\alpha]_D^{16}$ +57·4° (*c* 1·22) (Found: C, 80·4; H, 8·7; N, 5·3%). The identity of this product and the authentic nitrile was confirmed by comparison of their infrared spectra both in carbon disulphide solution and in Nujol.

(*B*) Sodium dehydroabietate was prepared by titration of aqueous ethanolic solutions of dehydroabietic acid (III; R = CO_2H) and sodium hydroxide to the phenolphthalein end-point. After removal of the solvents, the salt was dried thoroughly *in vacuo*.

The salt (620 mg.) was treated with cyanogen chloride under the conditions described in (*A*) above. Chromatography of the product (500 mg.) on deactivated alumina (75 g.) and elution with light petroleum (b. p. 40—60°) (150 ml.) gave an oil (79 mg.), ν 887 and 832 $cm.^{-1}$ (no bands due to C⋮N or C⋮O). The same solvent eluted successively: (with 200 ml.) an oil (62 mg.), ν 1724 $cm.^{-1}$; (with 100 ml.) a mixed fraction (28 mg.); and then (with 600 ml. solvent) dehydroabietonitrile (III; R = CN) (174 mg.), m. p. 78—85°. Recrystallized twice from hexane, the nitrile had m. p. 87—88° (Found: C, 85·3; H, 9·6. Calc. for $C_{20}H_{27}N$: C, 85·4;

[5] Campbell and Todd, *J. Amer. Chem. Soc.*, 1942, **64**, 928.
[6] Coleman, Leeper, and Schulze, *Inorg. Synth.*, 1946, **2**, 90.
[7] Sherwood and Short, *J.*, 1938, 1006.

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H, 9·6%), and it was shown to be identical with authentic dehydroabietonitrile (m. p. 87—88°) by the mixed m. p. test and by comparison of infrared spectra in carbon disulphide solution.

We are grateful to Professor E. Wenkert for a sample of dehydroabietonitrile. Maintenance Allowances are gratefully acknowledged from the Department of Scientific and Industrial Research (to A. C. D.) and the Medical Research Council (to D. B. B.). One of us (A. C. D.) thanks the Principal and Fellows of Brasenose College, Oxford, for the award of a Senior Hulme Scholarship.

Dyson Perrins Laboratory, Oxford University. [*Received, February 27th,* 1961.]

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624. *The Raman Spectra of Bis(trifluoromethylthio)mercury and Derived Compounds.*

By A. J. Downs, E. A. V. Ebsworth, and H. J. Emeléus.

The Raman spectra of bis(trifluoromethylthio)mercury, $Hg(S{\cdot}CF_3)_2$, in the molten state and in a variety of solvents have been recorded and analysed. The Raman effect has been used to compare the reactions in solution of this compound (*a*) with other mercuric salts, HgX_2 (where X = Cl, Br, I, or CN), and (*b*) with the corresponding tetramethylammonium or potassium salts, MX. Clear evidence has been obtained in (*a*) for the formation of derivatives of the type $CF_3{\cdot}S{\cdot}HgX$ in equilibrium with the reactants; the results from (*b*) are consistent with the formation of addition compounds of the type $M^+[Hg(S{\cdot}CF_3)_2X]^-$.

The properties of bis(trifluoromethylthio)mercury, $Hg(S{\cdot}CF_3)_2$, have recently been reported in some detail, but its Raman spectrum has not yet been published and the infrared spectrum has been incompletely described.[1,2] We have observed the Raman spectrum (over the range 100—1300 cm.$^{-1}$) of the mercury compound in the molten state, and also dissolved in benzene, carbon tetrachloride, ether, acetone, water, methanol and pyridine; in this paper the results are presented and interpreted. The complete infrared spectrum of the material is used, in conjunction with the Raman data, to make a partial frequency assignment. The molecule is presumably linear about the mercury atom and bent at each of the sulphur atoms, but since its symmetry is unknown, it is impossible to decide which of the 27 possible vibrational modes will be active in the infrared and Raman spectra. The observed spectra are incomplete and imperfectly resolved, so that any rigorous frequency assignment is out of the question; analysis has therefore been restricted to assignments to group frequencies rather than particular modes.

The Raman effect has been found particularly useful as a means of studying molecular species involved in labile chemical equilibria,[3] and we have applied this method to the study of the reaction of bis(trifluoromethylthio)mercury with mercuric chloride, bromide, iodide, and cyanide in solutions of methanol. The Raman spectrum of a particular mixture consists of a superposition of the spectra of the two pure compounds and, in addition, new lines not attributable to either of these; the new lines can be explained by the formation of the corresponding trifluoromethylthiomercuric halide in equilibrium with the reactants:

$$HgX_2 + Hg(S{\cdot}CF_3)_2 \rightleftharpoons 2CF_3{\cdot}S{\cdot}Hg{\cdot}X$$

Trifluoromethylthiomercuric chloride, which had been previously prepared and described,[2,4] was obtained by evaporating the solution and subliming the solid residue

[1] Man, Coffman, and Muetterties, *J. Amer. Chem. Soc.*, 1959, **81**, 3575.
[2] Pugh, M.Sc. Thesis, Cambridge, 1959.
[3] Woodward, *Quart. Rev.*, 1956, **10**, 185; François and Delwaulle, *J. Chim. phys.*, 1949, **46**, 80.
[4] Haszeldine and Kidd, *J.*, 1953, 3219; 1955, 3871.

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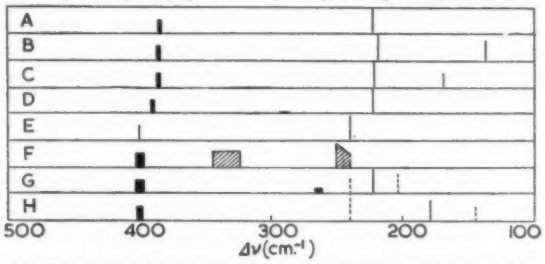
in a vacuum; attempts to isolate the corresponding bromide and iodide by similar methods led to recovery of the starting materials.

In direct contrast with such spectra are those of the products of reaction of bis(trifluoromethylthio)mercury with tetramethylammonium chloride, bromide, and iodide and with potassium cyanide. Earlier work has shown that bis(trifluoromethylthio)mercury reacts with tetramethylammonium chloride and iodide to give 1 : 1 adducts which have been formulated [5] as containing the complex anion $[Hg(S\cdot CF_3)_2X]^-$, where X is Cl or I. In the Raman spectra of acetone solutions of these compounds there is a marked lowering of the symmetrical Hg–S stretching frequency relative to the pure bis(trifluoromethylthio)-mercury, consistent with the formation of this anion. The formation of similar complexes between bis(trifluoromethylthio)mercury and tetramethylammonium bromide and potassium cyanide has been detected spectroscopically. An analogous frequency shift is found in the spectrum of a pyridine solution of the mercurial, in which complex-formation also takes place.[6] No unchanged bis(trifluoromethylthio)mercury was detected in such solutions, indicating that the complexes are not appreciably dissociated.

The experimental results may be summarised in the annexed line-diagram.

Raman spectra of bis(trifluoromethylthio)mercury and its derivatives.



Broken lines indicate scattering due to unchanged materials.

A, $Hg(S\cdot CF_3)_2$ *dissolved in pyridine.*
B, $NMe_4[Hg(S\cdot CF_3)_2I]$ *dissolved in acetone.*
C, $NMe_4[Hg(S\cdot CF_3)_2Br]$ *dissolved in acetone.*
D, $NMe_4[Hg(S\cdot CF_3)_2Cl]$ *dissolved in acetone.*
E, Pure $Hg(S\cdot CF_3)_2$ *dissolved in acetone or methanol.*
F, $Hg(S\cdot CF_3)_2 + HgCl_2$ (1 : 1) *dissolved in methanol.*
G, $Hg(S\cdot CF_3)_2 + HgBr_2$ (1 : 1) *dissolved in methanol.*
H, $Hg(S\cdot CF_3)_2 + HgI_2$ *dissolved in methanol.*

Results

A. *Vibrational Spectra of Bis(trifluoromethylthio)mercury.*—The observed frequencies of the infrared and Raman spectra of the pure compound are set out in Table 1, with the probable vibrational assignments and corresponding values for other trifluoromethyl compounds (where available).

There are numerous coincidences between the frequencies, but most of the skeletal modes are to be expected at frequencies well below the infrared range studied, so that there is no definite evidence in favour of a particular molecular symmetry. In most cases, assignments have been made by analogy, or with the help of the polarisation data. The intense and complex band in the infrared spectrum at 1080—1220 cm.$^{-1}$ must include all the C–F bond-stretching vibrations, and there is a corresponding broad but weak band in the Raman spectrum in this region; the comparatively feeble scattering is in keeping with the observed results [7] for CF_3Cl and is to be attributed to the low derived polarisability of the C–F bond. The band of medium intensity close to 750 cm.$^{-1}$ found in both spectra is a characteristic feature of the infrared

[5] Jellinek and Lagowski, *J.*, 1960, 810.
[6] Downs, unpublished work.
[7] Plyler and Benedict, *J. Res. Nat. Bur. Stand.*, 1951, **47**, 2245; Edgell and May, *J. Chem. Phys.*, 1954, **22**, 1808.

spectra of trifluoromethylthio-compounds [8] and is due to a coupled vibration involving both of the in-phase symmetrical CF_3 deformation and C–S stretching modes. On this basis the weak infrared band at 686 cm.$^{-1}$, with a very feeble Raman counterpart at 700 cm.$^{-1}$, has been assigned to the out-of-phase symmetrical CF_3 deformation. A similar pair of frequencies with almost the same separation is observed at 402 cm.$^{-1}$ (appearing as a relatively intense Raman line) and 467 cm.$^{-1}$ (a fairly weak band in both spectra). The stronger of these is complementary to the band near 750 cm.$^{-1}$, while the weaker is explained as arising from the out-of-phase C–S stretching vibration.

The line at 467 cm.$^{-1}$ is depolarised, and that at 402 cm.$^{-1}$ is polarised, in agreement with these assignments. There may be an infrared analogue to the strong Raman line at 400 cm.$^{-1}$, but it is so close to the limit of the range of the potassium bromide prism that no definite conclusion can be reached. The asymmetric CF_3 deformation, which has a frequency of 550—560 cm.$^{-1}$ in a wide range of trifluoromethyl compounds,[8] accounts for the weak infrared doublet

TABLE 1. *Infrared and Raman spectra of bis(trifluoromethylthio)mercury.*

Infrared (solid)		Raman (liquid)			
ν (cm.$^{-1}$)	Intensity, etc.	$\Delta\nu$ (cm.$^{-1}$)	Intensity, etc.	Assignment	Analogy
3650	w			3 × 1217	
2935	w			2 × 1123 + 686	
2860	w			2 × 1083 + 686	
2780	w sh			2 × (1103 or 1123) + 550	
2230	w br			2 × (1103 or 1123)	2210 in $(CF_3{\cdot}S)_2$
1453	w			1217 + 243	
1407	w			2 × ~700	
1369	w			1123 + 243	
1309	m			751 + 550	1300 in $(CF_3{\cdot}S)_2$
1217	m sh	1140			1208
1123	vs	to	vw br	ν CF (sym. and asym.)	1133 in $(CF_3{\cdot}S)_2$
1103	vs	1100			1109
1083	vs				1095
923	w sh			2 × 467	
751	m	755	m pol	δ CF_3 (sym., in-phase) (ν CS in-phase)	755 in $(CF_3{\cdot}S)_2$
686	w	~700	w br	δ CF_3 (sym., out-of-phase) (ν CS, out-of-phase)	
550, 542	w	~550	w br	δ CF_3 (asym.)	540 in $(CF_3{\cdot}S)_2$
467	w	465	w depol?	ν CS (out-of-phase) [δ CF_3 (sym., out-of-phase)]	468 in $CF_3{\cdot}SCl$
400?	,?	402	s pol	ν CS (in-phase) [δ CF_3 (sym., in-phase)]	
		343	w	CF_3 rock	356 in CF_3Cl
		243	vs pol	ν HgS (in-phase)	

Intensities, etc.: w = weak, m = medium, s = strong, v = very, sh = shoulder, br = broad; pol = polarised, depol = depolarised.

The terms "in-phase" and "out-of-phase" have been used to describe vibrations which are symmetric or antisymmetric with respect to the molecule as a whole, in order to avoid confusion with the symmetry of the vibrations within the CF_3-groups.

TABLE 2. *Strong lines in the Raman spectrum of bis(trifluoromethylthio)mercury in various solvents.*

	Frequencies (±2 cm.$^{-1}$)						
Vibration	CCl_4	C_6H_6	Acetone	Ether	MeOH	H_2O	Pyridine
δ CF_3 (sym., in-phase) [ν C–S (in-phase)]	755	755	~750	755	756	~760	755
ν C–S (in-phase) [δ CF_3 (sym., in-phase)]	402	401	400	399	400	400	383
ν Hg–S (in-phase)	243	243	241	240	240	239	223

and broad Raman band at about 550 cm.$^{-1}$. Similarly, the CF_3 rocking frequency of 356 cm.$^{-1}$ in CF_3Cl [7] suggests that the weak Raman line at 343 cm.$^{-1}$ is to be ascribed to this type of vibration. The very intense and polarised Raman line at 243 cm.$^{-1}$ is clearly to be assigned to

[8] Nabi and Sheppard, *J.*, 1959, 3439.

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the in-phase Hg–S stretching mode; in subsequent work, the presence of unchanged bis(trifluoromethylthio)mercury was determined by the scattering at this particular frequency. No line corresponding to the out-of-phase Hg–S stretching vibration could be detected; the pseudo-linear nature of the molecule may lead to its being very weak, if not actually forbidden, in the Raman spectrum. Possible skeletal bending and torsional frequencies are expected to be low and no Raman lines likely to be associated with these modes could be observed. The weak bands remaining in the infrared spectrum are interpreted as combinations of the fundamentals.

The frequencies of the three strongest Raman bands for a series of solutions of bis(trifluoromethylthio)mercury are listed in Table 2. The position of the bands is unaffected by the concentration for solutions up to 3M. The frequency of the Hg–S stretching vibration decreases on passing from inert solvents, such as carbon tetrachloride, to oxygen-containing donor solvents, such as methanol. This change is small but may be significant in view of the tendency of the mercurial to form adducts with donor molecules;[1] the effect is very much smaller than that observed with mercuric chloride, for which the frequency shifts have been related to the influence of solvation.[9] There is a large frequency change when pyridine is used as a solvent, in which complex-formation undoubtedly takes place.[6]

B. *Equilibria with Mercuric Salts.*—In solutions containing the mercurial and a mercuric halide or cyanide, the in-phase skeletal frequencies of the mercurial and mercuric salt, ν_{Hg-S} and ν_{Hg-X}, are usually accompanied in the Raman spectrum of the mixture by two new lines, ν^1_{Hg-S} and ν^1_{Hg-X}, both at rather higher frequencies than ν_{Hg-S} and ν_{Hg-X} respectively; under some conditions, the pairs may merge to give two broad bands which cannot easily be resolved. The position of the new lines does not depend upon the relative proportions of reactants, and the ratio of intensities of ν^1_{Hg-S} to ν^1_{Hg-X} is also the same for all proportions, but the relative intensities of ν_{Hg-S} to ν^1_{Hg-S} and of ν_{Hg-X} to ν^1_{Hg-X} depend upon the molar proportions of the reactants. Excess of mercuric halide causes ν_{Hg-S} to disappear, whereas excess of mercurial causes ν_{Hg-X} to disappear. The observed principal frequencies are set out in Table 3. The other bands in the spectra can be accounted for by the presence of bis(trifluoromethylthio)-mercury, although there are minor changes in the contours.

TABLE 3. *Strong Raman lines* (cm.$^{-1}$) *in spectra of methanol solutions containing equimolar concentrations of bis(trifluoromethylthio)mercury and a mercuric halide or cyanide.*

	$HgCl_2$		$HgBr_2$		HgI_2 *		$Hg(CN)_2$	
Frequency	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.
ν_{Hg-S}	240vs		240vs	—	240vs		240vs	
ν^1_{Hg-S}	251vs	253	264w	275	—	264	256w	259
ν_{HgX}	323s		204vs		145s		412w	
ν^1_{Hg-X}	243s	354	223vs	222	179s	176	—	425

* Solution contained excess of $Hg(S{\cdot}CF_3)_2$ because of the limited solubility of HgI_2.

For solutions containing mercuric cyanide, the expected weak fundamental ν^1_{Hg-X} could not be detected, but the line due to the pure cyanide at 274 cm.$^{-1}$ (w), arising from the Hg–C–N bending mode,[10] was accompanied by a new line at 298 cm.$^{-1}$ (w) to be ascribed to the corresponding mode of trifluoromethylthiomercuric cyanide: no new band associated with the C–N stretching vibration was observed.

For a molecule $CF_3{\cdot}S{\cdot}HgX$, there will be three skeletal modes of vibration involving, respectively, Hg–S·CF_3 stretching, Hg–X stretching, and deformation. All these modes are Raman-active, but the bending frequency is likely to be much the lowest and could not be detected in the present work. A rough calculation can be made of the two stretching frequencies corresponding to the two new Raman lines, ν^1_{Hg-S} and ν^1_{Hg-X}, by using the known values of the symmetrical stretching frequencies, ν_{Hg-S} and ν_{Hg-X}. For the pure mercury compounds (cf. ref. 11),

$$4\pi^2(\nu_{Hg-S})^2 = k_1/m_{SCF_3} \text{ and } 4\pi^2(\nu_{Hg-X})^2 = k_2/m_X \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where k_1 and k_2 are the force-constants, and m_{SCF_3} and m_X the appropriate masses of

[9] Allen and Warhurst, *Trans. Faraday Soc.*, 1958, **54**, 1786.
[10] Woodward and Owen, *J.*, 1959, 1055.
[11] Herzberg, "Infra-red and Raman Spectra of Polyatomic Molecules," Van Nostrand, New York, 1945, pp. 172, 173.

the trifluoromethylthio-group and halogen atom respectively. It is assumed that the force-constants are the same in the asymmetric molecule, the changes in frequency being purely a mass-effect. This is an over-simplification which can be justified only by the agreement between calculated and observed frequencies.[3] It can then be shown [11] that

$$(\nu^1_{Hg\text{-}S})^2 + (\nu^1_{Hg\text{-}X})^2 = (\nu_{HgS})^2\{1 + m_{SCF_3}/m_{Hg}\} + (\nu_{Hg\text{-}X})^2\{1 + m_X/m_{Hg}\} \quad . \quad . \quad (2)$$

and

$$(\nu^1_{Hg\text{-}S})^2(\nu^1_{Hg\text{-}X})^2 = [1 + (m_X + m_{SCF_3})/m_{Hg}]\ (\nu_{Hg\text{-}S})^2(\nu_{Hg\text{-}X})^2 \quad . \quad . \quad . \quad . \quad . \quad (3)$$

from which $\nu^1_{Hg\text{-}S}$ and $\nu^1_{Hg\text{-}X}$ can be calculated. For m_{SCF_3} the mass of the sulphur atom is used. Fair agreement with the observed frequencies is obtained despite the assumptions involved in the calculation.

A value for the equilibrium constant can be calculated in favourable cases from the relative intensities of the principal Raman lines of solutions containing various proportions of bis(trifluoromethylthio)mercury and the corresponding mercuric halide, by using the method described by François and Delwaulle.[3] For the system $Hg(S{\cdot}CF_3)_2 + HgBr_2 \rightleftharpoons 2CF_3{\cdot}S{\cdot}HgBr$, the equilibrium constant, K, given by

$$K = [CF_3{\cdot}S{\cdot}HgBr]^2/[Hg(S{\cdot}CF_3)_2][HgBr_2],$$

is $2{\cdot}3 \pm 0{\cdot}3$ at room temperature. In the equilibrium with mercuric chloride, the spectra do not lend themselves so well to this sort of calculation, the various Raman lines being less clearly resolved; the value of K is of the order of 20 (± 10). No such calculation could be made for the other mixtures.

C. *Adduct Formation.*—The Raman spectra of the pure tetramethylammonium compounds, $NMe_4[Hg(S{\cdot}CF_3)_2X]$ (X is Cl, Br, or I), have been recorded for saturated acetone solutions. Potassium cyanide gives a much less stable adduct which could not be isolated in the pure state; in this case, the spectrum of an acetone solution containing a mixture of the cyanide with a small excess of mercurial was observed. The frequencies are listed in Table 4.

TABLE 4. *Raman spectra of adducts of bis(trifluoromethylthio)mercury over the range* 100—800 cm.$^{-1}$.

$NMe_4[Hg(S{\cdot}CF_3)_2Cl]$ $\Delta\nu$ (cm.$^{-1}$)	$NMe_4[Hg(S{\cdot}CF_3)_2Br]$ $\Delta\nu$ (cm.$^{-1}$)	$NMe_4[Hg(S{\cdot}CF_3)_2I]$ $\Delta\nu$ (cm.$^{-1}$)	$K[Hg(S{\cdot}CF_3)_2CN]$ $\Delta\nu$ (cm.$^{-1}$)
		137vs	
	169s		
223vs	222vs	219vs	221vs
290wbr			
390s	386s	386s	388s
470w	465w		
650?vw			
690?vw			
751m *	750m *	751m *	

* This may include scattering due to the Me_4N^+ ion.

Most significant is the marked lowering in frequency of the in-phase Hg–S stretching vibration from 240 cm.$^{-1}$ (in solutions of the pure mercurial) to about 220 cm.$^{-1}$, a value close to that observed when the mercurial is dissolved in pyridine. This frequency varies little from compound to compound and seems to be characteristic of adducts of bis(trifluoromethylthio)-mercury. New bands at 290, 169, and 137 cm.$^{-1}$ in the spectra of the tetramethylammonium chloride, bromide, and iodide compounds, respectively, are ascribed to the Hg–X stretching vibration in the anion $[Hg(S{\cdot}CF_3)_2X]^-$. A smaller frequency shift (about 12 cm.$^{-1}$) was observed in the prominent Raman line associated with bis(trifluoromethylthio)mercury close to 400 cm.$^{-1}$, which tends to be much broader than in the spectrum of the pure mercury compound; the change in the overall molecular symmetry probably accounts for this. The scattering near 750 cm.$^{-1}$ is probably due both to the 750 cm.$^{-1}$ vibration of $CF_3{\cdot}S$ groups and also to the symmetrical " breathing " mode of the tetramethylammonium ion [12] at 752 cm.$^{-1}$. A number of missing bands are presumably too weak for detection in solutions of the concentrations used; no scattering could be assigned definitely to any of the frequencies characteristic of the tetramethylammonium ion [12] over the range 100—800 cm.$^{-1}$.

[12] Ebsworth and Sheppard, *Spectrochim. Acta*, 1959, **13**, 261.

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Analogous frequency shifts have been observed in the Raman spectra of mixed solutions of mercuric and alkali-metal halides, and correspond to the formation of the ions HgX_3^- and HgX_4^{2-};[13,14] the form of the spectrum depends on the molar ratio, R = HgX_2 : MX. When R exceeds 1, the spectrum contains a strong line associated with the symmetrical Hg–X stretching vibration of the HgX_3^- ion: when R is less than 0·5, this has shifted to a lower frequency corresponding to the formation of the HgX_4^{2-} ion. As R changes from 1 to 0·5, the band becomes broader and there is a continuous change in frequency of the centre between the two extreme values; in some cases, the band can be resolved into two components.[13] In the reaction of bis(trifluoromethylthio)mercury with tetramethylammonium halides, however, R cannot be made less than 1, since decomposition occurs under these conditions;[5] the ion $[Hg(S{\cdot}CF_3)_2X_2]^{2-}$ is evidently very unstable. For values of R greater than 1 the Raman spectrum of the solution contains, as expected, the bands characteristic of both the mercury compound and the complex.

The infrared spectra of the solid tetramethylammonium adducts have also been recorded over the range 400—4000 cm.$^{-1}$. Apart from the frequencies due to the tetramethylammonium ion and a change in the contour of the band associated with the C–F stretching mode, there is little essential difference between these spectra and that of pure bis(trifluoromethylthio)-mercury. In general, the spectra obtained give insufficient evidence for detailed analysis, and no definite conclusions can be reached concerning the molecular symmetry of the adducts.

Experimental

Bis(trifluoromethylthio)mercury was prepared by reaction between carbon disulphide and mercuric fluoride in an autoclave, and was purified by repeated vacuum-sublimation at room temperature and dried *in vacuo* over phosphorus pentoxide. The tetramethylammonium adducts were prepared by the method described by Jellinek and Lagowski.[5] For the solutions, dried " AnalaR " benzene, carbon tetrachloride, ether, acetone, methanol, and pyridine were used. Pure bis(trifluoromethylthio)mercury was examined in solutions of concentrations ranging from 0·3M to 3M. In all cases, the solutions were filtered through a fine glass sinter to obtain a suitably clear sample (4—5 ml.) for the Raman studies.

The Raman spectra were examined with a Hilger E612 spectrometer; the exciting line was the mercury line at 4358 Å. A filter consisting of a saturated aqueous solution of sodium nitrite was employed to suppress the primary lines of shorter wavelength; the level of background was such that no bands could be detected with any certainty within 120 cm.$^{-1}$ of the exciting line. The spectra were reproduced directly by means of a pen recorder operated by the amplified output from a photomultiplier unit. Qualitative determinations of the states of polarisation of the Raman lines were made by the method of polarised incident light,[15] successive records being taken with suitably oriented polaroid cylinders surrounding the sample-tube. Most of the solutions were colourless, but those containing mercuric iodide and the tetramethylammonium iodide adduct were tinted yellow; the slight colouring did not, however, appear to influence the spectra obtained. The observed frequencies were calibrated from the position of appropriate sharp bands in the spectra of pure carbon tetrachloride, benzene, and acetone, and are correct to within about ± 2 cm.$^{-1}$ for all but the weak and diffuse bands. The temperature of the samples was kept roughly constant by a water-cooled jacket surrounding the sample-tube, except in the case of pure bis(trifluoromethylthio)mercury, when the heat of the lamps was used to keep the material molten (m. p. 39°).

The infrared spectra were recorded at frequencies between 400 and 4000 cm.$^{-1}$ with a Perkin–Elmer model 21 double-beam spectrometer, fitted with a sodium chloride or potassium bromide prism. The compounds were examined as mulls with Nujol or hexachlorobutadiene.

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University Chemical Laboratory,
Lensfield Road, Cambridge. [*Received, December 19th*, 1960.]

[13] Delwaulle, François, and Wiemann, *Compt. rend.*, **206**, 1108.
[14] Delwaulle, *Bull. Soc. chim. France*, 1955, 1294; Rolfe, Sheppard, and Woodward, *Trans. Faraday Soc.*, 1954, **50**, 1275.
[15] Rank and Kagarise, *J. Opt. Soc. Amer.*, 1950, **40**, 89.

625. *Di*-p-(2-*amino*-2-*carboxyethyl*)*phenyl Peroxide*: *Preparation from Tyrosine and Probable Natural Occurrence in Proteins.*

By J. W. Davies and G. Harris.

The insolubilisation of certain proteins of barley and malt is probably due, among other causes, to the formation of a peroxide linkage between tyrosine residues of adjacent chains. In consequence 3-chlorotyrosine arises on hydrolysis of the insoluble protein by hydrochloric acid. By employing free tyrosine as a model the oxidation was simulated with hydrogen peroxide in hydrochloric acid to form di-*p*-(2-amino-2-carboxyethyl)phenyl peroxide. This compound is stable in solution only as the hydrochloride and on removal of or heating with hydrochloric acid yields 3-chlorotyrosine. Further treatment of the peroxide with hydrogen peroxide and hydrochloric acid gives successively the corresponding 3-chloro- and 3,5-dichloro-compound.

Chromatography on paper of concentrates of amino-acids obtained from brewer's wort by means of cation-exchange resins, revealed [1] the presence of an unidentified amino-acid, called compound X, occupying a position on two-dimensional chromatograms just below that of tyrosine. The same compound was observed in the hydrolysates of various proteins from malt, brewer's wort, and spent grains, and was particularly prominent in the less-soluble protein components as, for example, the deposits which separated when 70% ethanolic solutions of malt bynin (hordein) [2] were kept at 0°. The proteins in the solution then did not yield any significant amount of compound X on hydrolysis with hydrochloric acid, and the amount of the compound when it did arise was related inversely to that of tyrosine. Incidentally, the finding that compound X occurs mainly in the insoluble fractions affords an explanation of the fact that this amino-acid frequently appears as a product of the hydrolysis of the so-called protein hazes which form in malt products such as malt-extract, beer, and vinegar.

Starting with the knowledge that compound X gave, on paper chromatograms, colour reactions similar to those of tyrosine, and with the idea that its formation involved the oxidation of bound tyrosine, the oxidation of the free amino-acid was studied. Treatment of tyrosine with hydrogen peroxide or performic acid in hydrochloric acid afforded a crystalline product, m. p. 143° (decomp.), which behaved like compound X on chromatograms. However, the new product was unstable, being itself a powerful oxidising agent, and could not survive the conditions used to prepare compound X from wort or proteins. Nevertheless, on hydrolysis it yielded a stable compound occupying the same position on paper chromatograms and lacking oxidising properties. It seemed, therefore, that the primary unstable product, called compound X_1, might be a direct precursor of the stable compound X.

In similar studies, Thompson [3] identified 3-chlorotyrosine and 3,5-dichlorotyrosine among the products formed on hydrolysing, by means of hydrochloric acid, insulin which had been treated with performic acid.[4,5] The formation of these compounds was attributed to the presence, in the crude oxidation product, of hydrogen peroxide which liberated chlorine from the chloride present and so led to the chlorination of tyrosine (cf. Zeynek [6]). With this background compound X was soon identified with 3-chlorotyrosine.

The question arises as to how this chlorinated amino-acid can arise in worts and hydrolysates when it is derived from natural proteins in the absence of added oxidising

[1] Davies, Harris, and Parsons, *J. Inst. Brewing*, 1956, **62**, 38.
[2] Scriban, "Les Protides de l'Orge, du Malt et du Moût," Lille, 1951.
[3] Thompson, *Biochim. Biophys. Acta*, 1956, **15**, 440.
[4] Sanger, *Biochem. J.*, 1949, **44**, 126.
[5] Sanger and Tuppy, *Biochem. J.*, 1951, **49**, 463.
[6] Zeynek, *Z. physiol. Chem.*, 1925, **144**, 246.

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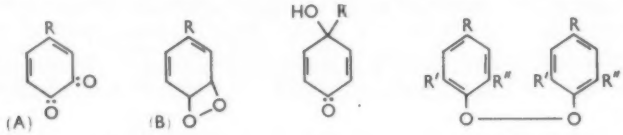
agents. It appeared that it might be formed from a precursor such as compound X_1, itself perhaps formed *via* a peroxidase known to be present in barley and malts.

Compound X_1 was an amino-acid hydrochloride, which had the empirical formula $C_9H_{14-16}ClNO_5$. Attempts to liberate the free base in solution resulted in the formation of 3-chlorotyrosine, a finding which explains the identical chromatographic behaviour of compound X and chlorotyrosine. Moreover, attempts to remove water of hydration completely brought about decomposition. Despite these difficulties the structure emerged from a consideration of the following evidence. In common with tyrosine it reacted with the formaldehyde–sulphuric acid reagent [7] and coupled with either 1-nitroso-2-naphthol or diazotised sulphanilic acid but, unlike tyrosine, gave no reaction with Millon's reagent. With the uranyl nitrate–benzene Rhodamine B reagent and with *o*-dinitrobenzene it reacted like a quinone while, unlike the original, it failed to liberate iodine from potassium iodide after treatment with *o*-phenylenediamine. Consideration was therefore given to structures such as " DOPA-3,4-quinone " (I) and toluquinol derivatives such as (II). It is interesting to observe that Earland and Stell [8] postulated the existence of a quinonoid derivative of tyrosine as an intermediate in the formation of insoluble proteins by the oxidation of silk fibroin while the formation of toluquinol [9] derivates by the oxidation of hindered phenols [10–12] is well known. However, comparison of the infrared and ultraviolet absorption spectra of compound X_1 with those of various quinones and semiquinones [7,11,13,14,15] (cf. Experimental) indicated that compound X_1 did not contain either a quinonoid or a semiquinonoid,[14,15] structure. Thus, it resembled tyrosine hydrochloride in having only a single sharp infrared absorption band (5·88 μ) in the region (5·8—6·0 μ) associated with carbonyl groupings, this band being due to the carbonyl of the undissociated carboxyl grouping, absent from the free base of tyrosine but present in the hydrochloride. The typical bands of toluquinol at 5·9—6·0 μ (conjugated carbonyl [13]) and 6·0—6·1 μ (conjugated ethylenic linkages) were absent.

In respect of its ultraviolet absorption, compound X_1 again resembled tyrosine rather than quinones or toluquinol as it had maximal absorption in aqueous acid at 280 mμ and in ethanol at 285 mμ whereas toluquinol, for example, shows absorption maxima at 277, 290, and 295 mμ.[13] In alkali it exhibited a principal absorption band at 300 mμ due to the formation of 3-chlorotyrosine. The " DOPA-quinone " structures (I) were ruled out, moreover, as compound X_1 lacks the typical 1,2-quinone infrared bands,[16] is colourless, and yields on catalytic reduction not DOPA but tyrosine. Taken in conjunction with the spectroscopic evidence, this shows that only one oxygen function is linked to the ring.



(I) (II) (III)

R = $CH_2 \cdot CH(CO_2H) \cdot NH_2$,HCl

Reaction of compound X_1 with potassium iodide showed that there was 0·5 active oxygen atom per nitrogen atom and that tyrosine was formed as the sole product rather

[7] Feigl, " Spot Tests in Organic Analysis," 5th edn., Elsevier, 1956.
[8] Earland and Stell, *Biochim. Biophys. Acta*, 1957, **23**, 97.
[9] Bamberger, *Ber.*, 1900, **33**, 3600; *Annalen*, 1912, **390**, 164.
[10] Bickel and Gersmann, *Proc. Chem. Soc.*, 1957, 231; Bickel and Kooyman, *J.*, 1953, 3211.
[11] Goodwin and Witkop, *J. Amer. chem. Soc.*, 1957, **79**, 179.
[12] Ley, *Angew. Chem.*, 1958, **70**, 74.
[13] Wessely and Sinwel, *Monatsh.*, 1950, **81**, 1055.
[14] Hathway, *J.*, 1957, 519.
[15] Hathway and Seakins, *Nature*, 1955, **176**, 218.
[16] Josien, *J. Chem. Phys.*, 1953, **21**, 331.

than chloro- or iodo-tyrosine, as might be expected from (II). Considering all the evidence, structure (III; R′ = R″ = H) best accommodates the facts. The ultraviolet absorption at 285 mμ recalls that of the analogous di-*p*-tolyl peroxide [17,18] while, in view of the lack of strong characteristic vibrations for peroxide groupings,[19] the infrared absorption is quite compatible with structure (III). The improbable formulations of compound X_1 as a simple hypochlorous acid salt, as a solvate containing hydrogen peroxide, or as a peracid can be discounted not only on the basis of the determination of active oxygen and the infrared absorption [19,20] but also because addition of 1 mole of hypochlorous acid, hydrogen peroxide, or a peracid to tyrosine failed to inhibit the Millon reaction.

Structure (III) accounts well for the formation of 3-chlorotyrosine from compound X_1 on neutralisation, presumably *via* hypochlorite. Under these conditions traces of DOPA are also formed and this product arises, together with its 2,3- and 2,5-isomers,[21] 3-chlorotyrosine, 3,5-dichlorotyrosine, tyramine, and complex coloured compounds, when compound X_1 is heated with water. The formation of coloured materials recalls the oxidative transformation of tyrosine into melanins.[22] In this connection, Onslow [23] suggested that peroxide derivatives of DOPA were intermediates which are converted subsequently into quinones and hence melanins. The present findings provide a chemical analogy for this suggestion.

The formation of peroxide units as in structure (III) in a protein would account among other reasons for the insolubilisation of the protein as a result of the cross-linking of the tyrosine residues of adjacent chains. Moreover, the solubilisation of such oxidised proteins by means of reducing agents might be explained by the fission of the peroxide cross-linkage. Whether or not the formation of 3-chlorotyrosine on hydrolysis of the oxidised protein by means of hydrochloric acid is then due to the intermediate formation of chlorine or to the isomerisation [25] of a transient derivative of phenyl hypochlorite remains undecided. An alternative possibility is that polyphenols associated with the protein undergo peroxidation and that the peroxide products themselves are responsible for the chlorination of tyrosine.

The reaction of compound (III) with hydrogen peroxide in alcoholic hydrochloric acid gave two further products having oxidising properties. Both compounds, called X_2 and X_3, resembled the original in that they (*a*) liberated iodine from potassium iodide, (*b*) gave no reaction with Millon's reagent, and (*c*) were isolable only as their hydrochlorides. When heated, treated with alkali, or on chromatography, compound X_2 gave rise to 3-chlorotyrosine while compound X_3 yielded 3,5-dichlorotyrosine. Compounds X_2 and X_3 had ultraviolet absorption characteristics like those of 3-chlorotyrosine and 3,5-dichlorotyrosine, respectively. In view of their derivation, composition, and properties, structures (III; R′ = H; R″ = Cl) and (III; R′ = R″ = Cl) are suggested for compounds X_2 and X_3, respectively.

Experimental

Chromatography of Amino-acids.—This was by ascending chromatography in a Datta frame.[1] The positions occupied by the various compounds on paper chromatograms are given in Table 1.

Hydrolysis of Proteins and Amino-acids.—Hydrolysis was carried out by use of 6N-hydrochloric acid at 100° for 16 hr. in the presence of Amberlite IR120, and the products were recovered from the resin.[1] Application of the method to tyrosine, 3-chlorotyrosine, or 3,5-dichlorotyrosine caused no change in these amino-acids.

[17] Wieland and Meyer, *Annalen*, 1942, **551**, 249.
[18] Breitenbach and Derkosch, *Monatsh.*, 1950, **81**, 530.
[19] Bellamy, "Infra-red Spectra of Complex Molecules," Methuen and Son, London, 1956.
[20] Davison, *J.*, 1951, 2456.
[21] Lissitsky and Roques, *Bull. Soc. Chim. biol.*, 1957, **39**, 521.
[22] Raper, *Biochem. J.*, 1926, **20**, 735; 1927, **21**, 1932, **26**, 2000.
[23] Onslow, *Biochem. J.*, 1923, **17**, 217.
[24] Lontie, Rondelet, and Dulcino, *European Brew. Conv. Proc.*, 1953, **33**.
[25] Likhosherstov and Arkhangel'skaya, *J. Gen. Chem. U.S.S.R.*, 1937, **7**, 1914.

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Protein Fractions from Barley, Malt and Spent Grains.—These were prepared by the methods described by Scriban.[3]

Compound X_1 (III; R′ = R″ = H).—Tyrosine (2·0 g.) in 2N-hydrochloric acid (10—12 ml.) and 30% hydrogen peroxide solution (8 ml.; Merck's Perhydrol) were kept at room temperature for 16—20 hr. The solution was evaporated in a vacuum by using a capillary and at below 30° until crystallisation set in. Ethanol was then added and evaporation continued with appropriate additions of ethanol until a dry residue was obtained. The solid was freed from residual

TABLE 1. $R_{Tyrosine}$ *values for tyrosine derivatives.*

Compound	Solvent	$R_{Tyrosine}$
3-Chlorotyrosine (X), di-*p*-(2-amino-2-carboxyethyl)phenyl-peroxide (X_1), and di-[4-(2-amino-2-carboxyethyl)-3-chlorophenyl]peroxide (X_2)	n-Butanol–acetic acid–water (4 : 1 : 1; v/v)	1·26
	Ethanol–2N-ammonia (9 : 1; v/v)	0·78
3,5-Dichlorotyrosine and di-[4-(2-amino-2-carboxyethyl)-3,5-dichlorophenyl] peroxide	n-Butanol–acetic acid–water (4 : 1 : 1; v/v)	1·58
	Ethanol–2N-ammonia (9 : 1; v/v)	0·46

solvent and excess of hydrogen chloride in a vacuum for 48 hr. and then extracted with cold ethanol. The solution was evaporated in a vacuum; the residue of *di*-p-(2-*amino*-2-*carboxyethyl*)*phenyl peroxide hydrochloride* crystallised from ethanol–ether as laths (1·6—1·7 g.), m. p. 143° (decomp.), $[\alpha]_D^{20}$ +12·9° (*c* 1·64 in EtOH) (Found: C, 42·9; H, 5·6; Cl, 13·4; N, 5·2. $C_{18}H_{22}Cl_2N_2O_6,4H_2O$ requires C, 42·8; H, 5·9; Cl, 14·1; N, 5·5%). Increasing the scale of the oxidation reduced the yield considerably.

The product contained 2 equiv. of amino-nitrogen as estimated by the van Slyke procedure [26] or Yemm and Cocking's colorimetric method.[27] Heating with 6N-hydrochloric acid or treatment with 1 mole of N-sodium hydroxide or N-sodium carbonate yielded 3-chlorotyrosine, m. p. and mixed m. p. 261—263° (decomp.) (Found: C, 46·5; H, 5·3; Cl, 15·3; N, 6·3. Calc. for $C_9H_{10}ClNO_3,H_2O$: C, 46·3; H, 5·1; Cl, 15·3; N, 6·0%). The final solution in each case, and particularly after treatment with sodium hydroxide, on hydrogenation contained in addition a small amount of 3,4-dihydroxyphenylalanine as revealed by chromatography in the solvent system butanol–acetic acid–water (4 : 1 : 1, v/v), and spraying of the final chromatogram with 2,6-dichloroquinone-4-chloroimide,[28] a reagent which is specific for 1,2-dihydroxybenzene derivatives in this series.

The peroxide (III) was put on to Whatman No. 3 MM papers, and the chromatogram developed with butanol–acetic acid–water. The zone reactive to ninhydrin was eluted from the dried papers with water, the solution concentrated, and the residue crystallised from acetic acid to yield 3-chlorotyrosine, m. p. and mixed m. p. 264°.

The results of spot tests [7] on (III; R′ = R″ = H) are listed in Table 2.

3-*Chlorotyrosine*.—The hydrochloride, m. p. 240°, was prepared as described by Zeynek [6] and converted into the free base, m. p. 264° (decomp.). It gave a positive reaction with Millon's reagent and failed to liberate iodine from potassium iodide.

3,5-*Dichlorotyrosine*.—The hydrochloride,[29] m. p. 246°, gave a negative reaction with Millon's reagent but did not liberate iodine from potassium iodide.

Catalytic Reduction of (III; R′ = R″ = H).—The compound was hydrogenated in water in the presence of palladium. Chromatography of the filtrate revealed the presence of only tyrosine. Evaporation of the solution and crystallisation of the residue from ethanol–ether gave tyrosine hydrochloride, m. p. 227—230° (Found: N, 6·4. Calc. for $C_9H_{11}NO_3,HCl$: N, 6·3%). With Adams' catalyst in place of palladium, only 3-chlorotyrosine was formed.

Reaction of (III; R′ = R″ = H) *with Potassium Iodide*.—The compound (8·74 mg.) was set aside for 10 min. with excess of potassium iodide in hydrochloric acid. The liberated iodine was titrated with sodium thiosulphate and corresponded to one active oxygen per 2 nitrogen atoms (Found: 3·2, 3·3; required 3·2%). Chromatography of the solution revealed the presence of tyrosine, which was worked up by means of Amberlite IR120. Corresponding

[26] Van Slyke, McFadyen, and Hamilton, *J. Biol. Chem.*, 1941, **141**, 671.
[27] Yemm and Cocking, *Analyst*, 1955, **80**, 209.
[28] Harris, *J. Inst. Brewing*, 1956, **43**, 390.
[29] Bouchilloux, *Bull. Soc. Chim. biol.*, 1955, **37**, 255.

solutions which had not been treated with potassium iodide yielded only 3-chlorotyrosine when worked up in the same way.

Preparation of Model Quinones, Semiquinones, and Peroxides.—*p*-Benzoquinone and *p*-toluquinone,[30] 2,2-diacetoxy-4-methylcyclohexa-3,5-dien-1-one, 4-acetoxy-4-methylcyclohexa-2,5-dien-1-one, *p*-toluquinol [11] and di-*p*-tolyl peroxide [17] were made according to literature methods.

Oxidation [30] *of Compound* (III; R′ = R″ = H).—The compound (0·38 g.) in 10% sulphuric acid (10 ml.) was treated with potassium permanganate (0·75 g.), and the mixture warmed for 10 min. Sodium hydrogen sulphite was added to discharge the colour, the mixture was extracted with ether, and the ethereal solution evaporated to dryness. The product was identified by chromatography as *p*-coumaric acid.[31]

TABLE 2. *Results of spot tests* [7] *on compound* X_1.

Reagent	Test for	Result: Tyrosine	Result: Compound X_1
Formaldehyde–sulphuric acid	Aromatic nucleus	+	+
Ehrlich reagent	Coupling	+	+
Uranyl nitrate–benzene Rhodamine B	–CO·CO– or CH_2·CO–	—	+
Potassium iodide	–CO– or	—	+
Potassium iodide after *o*-phenylenediamine	–CO·CO–	—	—
o-Dinitrobenzene	–CO·CO– and quinones	Indef.	+
Pyrolysis		Odour of burned hair	Odour of chlorine
Millon reagent	*p*-Substituted phenols	+	—
Sodium nitroprusside–aldehyde	–NH–	—	—
p-Dimethylaminobenzaldehyde	Indole	—	—
Sodium hypochlorite–Fuchsin–sulphurous acid	R·CH(NH_2)·CO_2H	+	+
Thionyl chloride–hydroxylamine–sodium hydroxide	$–CO_2H$	+	+
Ferric chloride–potassium ferricyanide	Phenol	+	+

Action of Hot Water on Compound (III; R′ = R″ = H).—The peroxide (0·8 g.) in water (50 ml.) was heated under reflux for 0·5 hr. The solution was concentrated in a vacuum and the product chromatographed in butanol–acetic acid–water to reveal 3-chlorotyrosine, tyrosine, tyramine, and dihydroxyphenylalanines. Similar heating of tyrosine, monochlorotyrosine, and dichlorotyrosine yielded only starting materials.

Compound X_2.—Compound (III; R′ = R″ = H) (5·36 g.) was dissolved in ethanol (100 ml.) and sufficient 2N-hydrochloric acid to complete solution. Perhydrol (20 ml.) was added and the mixture worked up as described above for the starting material. Crystallisation from ethanol–ether yielded *di*-[4-(2-*amino*-2-*carboxyethyl*)-3-*chlorophenyl*] *peroxide dihydrochloride* (III; R′ = H, R″ = Cl) as needles, m. p. 130° (decomp.), $[\alpha]_D^{20}$ +12·6° (*c* 1·288 in ethanol) (Found: C, 39·5; H, 4·9; Cl, 25·6; N, 5·2. $C_{18}H_{20}Cl_4N_2O_6,2H_2O$ requires C, 40·1; H, 4·5; Cl, 26·4; N, 5·2%). Treatment of the ground solid with 1 mole of ethereal diazomethane yielded 3-chlorotyrosine.

Compound X_3.—Compound (III; R′ = R″ = H) (1·05 g.) was dissolved in ethanol (10 ml.) and 2N-hydrochloric acid (12 ml.), and the solution treated with perhydrol (8 ml.). After 24 hr. the solution was evaporated as above. The orange solid was washed with ethanol–ether and dried in a vacuum to give *di*-[4-(2-*amino*-2-*carboxyethyl*)-3,5-*dichlorophenyl*] *peroxide dihydrochloride* (III; R′ = R″ = Cl), m. p. 98° (Found: C, 35·9; H, 3·9; Cl, 35·6; N, 4·3. $C_{18}H_{18}Cl_6N_2O_6,2H_2O$ requires C, 35·6; H, 3·6; Cl, 35·1; N, 4·6%).

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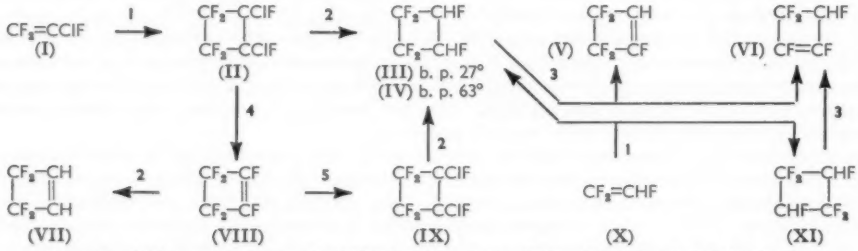
626. *Some Isomeric Hexafluorocyclobutanes and Pentafluorocyclobutenes.*

By G. Fuller and J. C. Tatlow.

Re-examination of the reaction of lithium aluminium hydride with 1,2-dichlorohexafluorocyclobutane showed that both the known 1*H*,2*H*-hexafluorocyclobutane, b. p. 27°, and a new 1*H*,2*H*-isomer, b. p. 63° were formed. On dehydrofluorination, each 1*H*,2*H*-hexafluorocyclobutane gave principally 1*H*-, and a little 3*H*-pentafluorocyclobutene. High-pressure dimerisation of trifluoroethylene gave a mixture of four products, of which the two 1*H*,2*H*-hexafluorocyclobutanes, and a 1*H*,3*H*-hexafluorocyclobutane, b. p. 38°, have been identified. The last, on dehydrofluorination, gave only 3*H*-pentafluorocyclobut-1-ene which was oxidised to trifluorosuccinic acid. With lithium aluminium hydride, hexafluorocyclobutene gave 3,3,4,4-tetrafluorocyclobut-1-ene.

Thermal dimerisation of fluoroethylenes to give fluorocyclobutanes is well established,[1-5] one of the best known examples [2-5] being the conversion of chlorotrifluoroethylene (I) into 1,2-dichlorohexafluorocyclobutane (II). The latter resembled other chlorofluorocarbons [6,7] in its reaction with lithium aluminium hydride in diethyl ether, the chlorine being completely replaced by hydrogen.[8] Only one fluorohydrocarbon was isolated, a 1*H*,2*H*-hexafluorocyclobutane (III), having b. p. 27°. We now report a re-examination of this reaction which has shown that, besides compound (III), another 1*H*,2*H*-compound (IV), with b. p. 63°, is formed as well. Compound (IV) was isolated by gas chromatography, which was not available when the earlier work [8] was done.



Reagents: 1, Heat and pressure. 2, $LiAlH_4$ in Et_2O. 3, Aq. KOH. 4, Zn dust in EtOH. 5, Cl_2.

Electron-diffraction studies [9] of octafluorocyclobutane have shown that the ring is puckered. Presumably, however, interconversion of conformations occurs and isomers will arise as from a planar ring. There should be two stereoisomers of a derivative of the type 1,2-$C_4F_6X_2$ and the *trans*-isomer should exist in D- and L-forms. Where the substituents are chlorine or hydrogen, however, no ready means is available for resolving such a racemate. *cis*- and *trans*-Forms of 1,2-dichlorohexafluorocyclobutane have been obtained previously.[10] The usual route to this compound is thermal dimerisation of chlorotrifluoroethylene (I); when this dimer (II) was dechlorinated with zinc dust, and the

[1] Coffman, Barrick, Cramer, and Raasch, *J. Amer. Chem. Soc.*, 1949, **71**, 490.
[2] Harmon, U.S.P. 2,404,374/1946.
[3] Henne and Ruh, *J. Amer. Chem. Soc.*, 1947, **69**, 279.
[4] Lacher, Tompkin, and Park, *J. Amer. Chem. Soc.*, 1952, **74**, 1693.
[5] Buxton, Ingram, Smith, Stacey, and Tatlow, *J.*, 1952, 3830.
[6] Tatlow and Worthington, *J.*, 1952, 1251.
[7] Smith and Tatlow, *J.*, 1957, 2505.
[8] Buxton and Tatlow, *J.*, 1954, 1177.
[9] Lemaire and Livingston, *J. Amer. Chem. Soc.*, 1952, **74**, 5732.
[10] Lacher, Büchler, and Park, *J. Chem. Phys.*, 1952, **20**, 1014.

hexafluorocyclobutene (VIII) so formed was treated with chlorine, another sample of dichloride (IX) was obtained. After further purification these dichlorides (II and IX) had slightly different physical properties, the higher-boiling thermal dimer (II) being allocated [10] the *cis*- and the lower-boiling chlorine adduct (IX) the *trans*-structure. Later work [11] has indicated that the crude thermal dimer is a mixture of nearly equal proportions of *cis*- and *trans*-isomers.

In the present work, we repeated the previously reported [8] reaction of 1,2-dichlorohexafluorocyclobutane (II) (prepared by thermal dimerisation of chlorotrifluoroethylene) with lithium aluminium hydride in diethyl ether, using analytical and preparative gas chromatography in the isolation of the products. As before, virtually all the chlorine was removed, and 1*H*,2*H*-hexafluorocyclobutane (III), b. p. 27°, was isolated in about 35% yield. A second product (IV), b. p. 63° (*ca.* 30% yield), was isolated from the high-boiling residues left after distillation of the solvent.

This product (IV) was shown to be a 1*H*,2*H*-hexafluorocyclobutane by dehydrofluorination with aqueous potassium hydroxide. A mixture of two monounsaturated products was obtained; these were separable only with great difficulty by preparative-scale gas chromatography. The major one was 1*H*-pentafluorocyclobutene (V), obtained previously [8] by an analogous reaction with the first hexafluoride (III). The other (<20%) was 3*H*-pentafluorocyclobutene (VI), since it had an infrared band at 1795 cm.$^{-1}$ from a −CF=CF− group [cf.[12] the band from hexafluorocyclobutene (VIII) at 1799 cm.$^{-1}$ and that from the −CH=CF− group of the 1*H*-isomer (V) at 1685 cm.$^{-1}$]. Infrared spectroscopy showed that the sample of 1*H*-pentafluorocyclobutene (V) obtained in the previous work had contained a little of the new olefin (VI). This was suspected before but could not be proved. Repetition of the dehydrofluorination of compound (III) confirmed that a few percent of compound (VI) was contaminating the major product (V). Mass-spectroscopic investigations were carried out by Dr. J. R. Majer [13] on compounds (III), (IV), and (VI) and supported the structures allocated to them.

The action of ethereal lithium aluminium hydride on 1,2-dichlorohexafluorocyclobutane (IX) prepared by chlorine addition was next studied. A sample was made essentially by the method used by the previous authors; [10] both it (IX) and the thermal dimer (II) had the infrared spectra described.[10] However, with ethereal lithium aluminium hydride the chlorine adduct (IX) gave the two hexafluorocyclobutanes in proportions (III, 31%; IV, 36%) similar to those (III, 37%; IV, 31%) obtained from the dimer (II). In view of the difficulties of isolation little significance can be attached to the small differences in proportions. It seems that some *cis–trans*-interconversion must occur in the reactions of the dichlorocyclobutanes (II and IX) with lithium aluminium hydride. Even if the *cis*- and the *trans*-dichloride were not so pure as was suggested,[10] complete retention or complete inversion of configuration should have given bigger differences in the proportions of the products (III and IV) obtained. It is possible that complete interconversion occurred. In the cyclohexane field, the chlorine adducts of decafluorocyclohexene [7] and of 4*H*-nonafluorocyclohexene [14] were treated with lithium aluminium hydride. In each case, the dichloride was of unknown configuration, but the product contained more *cis*- than *trans*-1*H*,2*H*-compound [(i) 72% 1*H*,2*H*/-, and 28% 1*H*/2*H*-decafluorocyclohexane; [7] (ii) 75% 1*H*,2*H*,4*H*/- + 1*H*,2*H*/4*H*-, and 25% 1*H*,4*H*/2*H*- + 1*H*/2*H*,4*H*-nonafluorocyclohexane [14]].

Unequivocal allocation of structure to compounds (III) and (IV) is not yet possible. The difference in boiling points (36°) between them is considerable; for the analogous 1*H*,2*H*-decafluorocyclohexanes [7] it is 21°. In the cyclohexane series it seems that a stereoisomer with hydrogen atoms close together in space has a higher boiling point and a longer retention time in gas chromatography than one where they are further apart. On

[11] Park, Holler, and Lacher, *J. Org. Chem.*, 1960, **25**, 990.
[12] Burdon and Whiffen, *Spectrochim. Acta*, 1958, **12**, 139.
[13] Majer, "Advances in Fluorine Chemistry," Butterworths, London, 1961, Vol. II, p. 55.
[14] Stephens, Tatlow, and Wiseman, *J.*, 1959, 148.

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this basis, compound (III) should be the *trans*- and compound (IV) the *cis*-isomer. In contrast, from the arguments on dehydrofluorination developed in the cyclohexane series,[7,14] it might be expected that the *cis*- would give less 3*H*-pentafluorocyclobutene (VI) than the *trans*-isomer. Experimentally, the higher-boiling hexafluoride (IV) gave rather more than the other (III). However, qualitatively there appeared to be a much smaller difference between the rates of elimination of these stereoisomers (III and IV) than there was with the analogous [7] cyclohexanes, 1*H*/2*H*- and 1*H*,2*H*/-decafluorocyclohexane. Compound (IV) appeared to be more reactive, but both were dehydrofluorinated completely at room temperature with no starting material left (cf. *trans*-1*H*,2*H*-decafluorocyclohexane [7]). The geometry of the cyclobutane ring will make the operation of a rigid planar *trans*-elimination mechanism more difficult for this ring system than for cyclohexanes. Nevertheless, elimination occurs quite readily. It is possible that because of the strain in the cyclobutane ring system, elimination processes not normally favoured, for example involving carbanions, can operate. If the allocation of structure [10] to the 1,2-dichlorohexafluorocyclobutanes is correct, then the higher-boiling stereoisomer (the thermal dimer II) is *cis*, and the lower-boiling one (IX) is *trans*. The former gave slightly more of the lower-boiling 1*H*,2*H*-compound (III), and the latter (IX) gave slightly more of the other isomer (IV). If these proportions of products are significant then there is a discrepancy, but it seems much more probable that *cis–trans*-interconversion occurred and that equal amounts of the two dihydro-compounds were formed in each case. Thus, though compound (III) is most likely to be *trans*, and compound (IV) *cis*, a final decision must await measurements of dipole moments.

The isolation of two compounds (III and IV) after reaction of lithium aluminium hydride with the dichlorides (II and IX) has possible repercussions on other work. Perfluorocyclobutene (VIII) has been treated [15] with bromine, chlorine, iodine chloride, and hydrogen bromide. In each case the addition product was reduced with ethereal lithium aluminium hydride to give compound (III) in yields varying from 51% to 74%, which were stated to be low owing to difficulties of isolation. As in our earlier work,[8] the isomer (IV) was not detected, but it seems very likely that some was present. When the fluorocarbon (VIII) was treated [16] with hydrogen iodide, a compound of b. p. 63—65° was formed to which the structure 1,1,2,3,4,4-hexafluorobutane was allocated. The authors stated that the product expected by hydrogen addition (*i.e.*, III) was not produced, but the new compound (IV) with very similar properties to those of the material isolated could have been, and could have contaminated the product.

Other possible routes to unsaturated derivatives of cyclobutane were investigated in the present work. On further treatment of the cyclobutene (VI) with alkali, there was no evidence of the formation of a cyclobutadiene derivative. Passage of hexafluorocyclobutene (VIII) over heated metal gauze in the apparatus used [17] for the defluorination of fluoro-cyclohexenes and -cyclohexanes to aromatic fluoro-compounds also failed to give a cyclobutadiene, no reaction or complete degradation resulting. The perfluoro-compound (VIII) reacted with ethereal lithium aluminium hydride in the same way as fluorocyclohexenes do.[18] The product was 3,3,4,4-tetrafluorocyclobutene (VII), as shown by oxidation to tetrafluorosuccinic acid and by addition of bromine to give a 1,2-dibromo-adduct. The −CH=CH− group had a characteristically [12] very weak infrared band; it is possible to overlook, in the spectrum of a fluoro-olefin, absorption due to a double bond of this type. A two-fold addition–elimination process of the type postulated before [18] appears to explain this reaction of olefin (VIII). Under the conditions used the supposed primary product 1*H*-pentafluorocyclobutene (V) must itself be sufficiently reactive to give the dihydro-compound (VII). This, however, would be appreciably less reactive towards

[15] Haszeldine and Osborne, *J.*, 1956, 61.
[16] Haszeldine and Osborne, *J.*, 1955, 3880.
[17] Gething, Patrick, Stacey, and Tatlow, *Nature*, 1959, **183**, 588.
[18] Nield, Stephens, and Tatlow, *J.*, 1960, 3800.

lithium aluminium hydride, as happens in other series [18] with increasing numbers of hydrogen atoms on the vinylic or α-carbon atoms. Since this work was done the preparation of 3,3,4,4-tetrafluorocyclobutene (VII) by dehydrobromination of 3-bromo-1,1,2,2-tetrafluorocyclobutane (made from tetrafluoroethylene and vinyl bromide) has been described.[11]

Thermal dimerisation of trifluoroethylene (X) is another route to polyfluorocyclobutanes; it has been attempted before [11] but without success. Trifluoroethylene (X) was prepared [19] from chlorotrifluoroethylene (I). It was very resistant to cyclo-dimerisation, but after being heated in an autoclave at 260° for 23 hr., it had formed a liquid product. This was shown by gas chromatography to contain 4 components, which were separated by preparative-scale gas chromatography. The first was a trace of unchanged olefin (X) and the second had an infrared spectrum identical with that of 1*H*,2*H*-hexafluorocyclobutane (III). The third was a new compound (XI), and the fourth was shown by infrared spectroscopy to be a mixture of roughly equal proportions of the 1*H*,2*H*-isomer (IV) and a second new compound. Analysis, mass spectrometry, and infrared spectroscopy suggested that compound (XI) was a 1*H*,3*H*-hexafluorocyclobutane. This was confirmed by dehydrofluorination with aqueous potassium hydroxide, the sole product being 3*H*-pentafluorocyclobutene (VI), identical with the material obtained previously. This product (VI) should also be a racemic mixture, but resolution would be difficult. Isolation of the cyclobutene (VI) on a larger scale than hitherto enabled its structure to be confirmed. With bromine, a dibromo-adduct was formed, and oxidation with potassium permanganate in acetone gave trifluorosuccinic acid. This was identified as its dianilinium salt which has been made recently [20] from acid obtained by reduction of chlorotrifluorosuccinic acid with zinc. The second new compound could not be separated from compound (IV). It was probably the other stereoisomer of 1*H*,3*H*-hexafluorocyclobutane (XI); the infrared spectrum was in accord with this, but proof must await its separation. Thus it appeared that cyclo-dimerisation of trifluoroethylene gives all four possible products, and in roughly comparable amounts. It is now apparent that additions to unsymmetrical fluoro-olefins do not always proceed exclusively in one direction, and trifluoroethylene gives [21] both products from free-radical addition reactions. It was shown recently [22] that hexafluoropropene can be cyclo-dimerised under drastic conditions, three perfluoro(dimethylcyclobutanes) being isolated. So far as we are aware, homo-dimerisation of a fluoro-olefin to a cyclobutane has been reported only for compounds containing a $>CF_2$ group, and it now appears that these groups in the two reactant molecules do not in all cases have to join up to give a product containing a $-CF_2-CF_2-$ residue.

Experimental

Reduction of 1,2-*Dichlorohexafluorocyclobutane* (II) (*Thermal Dimer*).—The dichloride was prepared from chlorotrifluoroethylene in an autoclave as before; [5] the infrared spectrum was the same as that published.[10] The compound (II) (30·0 g.) was added during 25 min. to a stirred suspension of lithium aluminium hydride (7·9 g.) in diethyl ether (200 c.c.), cooled by ice, under a reflux condenser cooled in solid carbon dioxide–ethanol. After 1¾ hr. at 0°, water (20 c.c.) was added, followed by 12N-sulphuric acid (75 c.c.) and more water (150 c.c.). The aqueous phase contained chloride ion corresponding to 94% of the original organic chlorine. The ether layer and ethereal extracts of the aqueous phase were dried ($MgSO_4$) and fractionally distilled (4′ column packed with nickel gauzes) to give fractions (i) (11·0 g.), b. p. 27·5—32°, (ii) (14·5 g.), b. p. 33·0—33·5°, and (iii) (15·0 g.), b. p. 33·5°. Distillation was continued through a 1′ column to give (iv) b. p. 33·9°, and (v) (13·5 g.), the still residue. Fraction (iv) was ether and (iii) was ether containing only a trace of product.

Fractions (i) and (ii) were separated by preparative-scale gas chromatography (column A

[19] Park, Sharrah, and Lacher, *J. Amer. Chem. Soc.*, 1949, **71**, 2339; Park, Lycan, and Lacher, *J. Amer. Chem. Soc.*, 1951, **73**, 711.
[20] Raasch, Miegel, and Castle, *J. Amer. Chem. Soc.*, 1959, **81**, 2678.
[21] Haszeldine and Steele, *J.*, 1957, 2800.
[22] Hauptschein, Fainberg, and Braid, *J. Amer. Chem. Soc.*, 1958, **80**, 842.

of ref. 14, temp. 58°, N_2 flow rate 8·3 l./hr., 3 portions) to give 1*H*,2*H*-hexafluorocyclobutane (III) (7·7 g.) and ether. Compound (III) had b. p. 27°, $\nu_{max.}$ 2986 cm.$^{-1}$ (>C–H); mass spectrometry gave principal mass peaks 164 very small ($C_4H_2F_6$), 100 (C_2F_4), 95 ($C_3H_2F_3$), 82 (C_2HF_3), 64 ($C_2H_2F_2$). The compound was identical with that isolated before.[8] The still residue (v) was separated by gas chromatography (column A, temp. 86°, N_2 flow rate 8·5 l./hr., 2 portions) into ether and 1H,2H-*hexafluorocyclobutane* (IV) (6·5 g.), b. p. 62·5—63·5°, n_D^{19} 1·2974, $\nu_{max.}$ 3012, 2973 cm.$^{-1}$ (>C–H) (Found: C, 28·9; H, 1·3; F, 69·0. $C_4H_2F_6$ requires C, 29·3; H, 1·2; F, 69·5%). Mass spectrometry gave principal mass peaks 164 vanishingly small ($C_4H_2F_6$), 144 small (C_4HF_5), 131 small (C_3F_5), 126 small ($C_4H_2F_4$), 100 (C_2F_4), 95 ($C_3H_2F_3$), 82 (C_2HF_3), 64 ($C_2H_2F_2$).

Preparation and Reduction of 1,2-*Dichlorohexafluorocyclobutane* (IX) (*Photochemical Adduct*).—Hexafluorocyclobutene [5] (23·0 g.) and chlorine (22·0 g.) in a hard-glass tube surmounted by a reflux condenser cooled in solid carbon dioxide–ethanol were irradiated with light from a high-pressure mercury lamp (G.E.C. " Osram," 125 w, black glass). After 6 hr., the residual liquid was washed with 10% aqueous sodium hydrogen carbonate and dried ($MgSO_4$). It was combined with the product from a similar experiment on hexafluorocyclobutene (16·0 g.) and fractionally distilled (6" column) to give 1,2-dichlorohexafluorocyclobutane (IX) (32·0 g.), b. p. 58·5—59·3°, n_D^{21} 1·3330. The infrared spectrum was similar to that given previously.[10] The band at 1021 cm.$^{-1}$ was stronger and those at 1050 and 890 cm.$^{-1}$ much weaker than those from the thermal dimer.

This dichloride (IX) (30 g.) was treated with lithium aluminium hydride in diethyl ether under conditions identical with those described for the reduction of the thermal dimer (II). Isolation as before gave 1*H*,2*H*-hexafluorocyclobutane (III), b. p. 27° (6·6 g.), and the stereoisomer (IV), b. p. 63° (7·6 g.), having infrared spectra identical with those of the corresponding samples from the previous experiment.

Dehydrofluorination of 1H,2H-*Hexafluorocyclobutane* (IV).—Compound (IV) (35·0 g.) and potassium hydroxide (70 g.) in water (50 c.c.) at 19° were stirred for 3¾ hr. (after 30 min. the temperature of the mixture exceeded 30° and intermittent cooling was necessary to control the refluxing). The mixture was cooled, and then separated in an ice-cold funnel, and the organic layer (20·6 g.) was washed quickly with ice-cold water. Analytical gas chromatography showed virtually no starting material, but the peak due to the known [8] 1*H*-pentafluorocyclobutene (V) had an inflexion on its leading edge. Preparative-scale gas chromatography [14] (column B, temp. 27°, N_2 flow rate 56 l./hr.) gave three fractions, (*a*) (2·0 g.), (*b*) (8·2 g.), and (*c*) (6·4 g.). Further preparative-scale gas chromatography on fraction (*a*) (column A, temp. 34°, N_2 flow rate 5·8 l./hr.) gave a sample (0·8 g.) of 3H-*pentafluorocyclobutene* (VI) [Found: *M*, 144 (by mass spectrometry). C_4HF_5 requires *M*, 144], $\nu_{max.}$ 1795 (–CF=CF–) and 2988 cm.$^{-1}$ (>C–H). Mass spectrometry gave principal mass peaks 144 (C_4HF_5), 125 (C_4HF_4), 94 (C_3HF_3), 93 (C_3F_3), 82 small (C_2HF_3) and 62 small (C_2F_2); the stable peak at 100 (C_2F_4) was virtually absent.

Further purification (column B, temp. 32°, N_2 flow rate 46 l./hr.), was carried out on fraction (*c*). The final part of the material was 1*H*-pentafluorocyclobutene (V) which had $\nu_{max.}$ 1673 (–CF=CH–) and 3143 cm.$^{-1}$ (>C–H) with no detectable bands due to the 3*H*-isomer (VI).

Infrared measurements on the original mixture showed the presence of 15—20% of the 3*H*-cyclobutene (VI).

Dehydrofluorination of 1H,2H-*Hexafluorocyclobutane* (III).—Compound (III) (15·2 g.) was dehydrofluorinated as described before.[8] Infrared spectroscopy and analytical gas chromatography of the product (9·5 g.) revealed 1*H*-pentafluorocyclobutene (V) containing the 3*H*-isomer (VI) (<10%).

Dimerisation of Trifluoroethylene.—This olefin (14·5 g.) was condensed in a test-tube cooled by liquid air. The tube was then rapidly put into an autoclave (120 c.c. capacity) which was assembled quickly. After being heated at 260° for 23 hr. (50—60 atm.), the vessel was cooled and opened, volatile material (6·5 g.) escaping. The liquid residue (7·5 g.) showed 4 peaks on analytical gas chromatography over 1 : 2 dinonyl phthalate–kieselguhr (temp. 82°, N_2 flow rate 0·8 l./hr.), but over trifluoroacetic acid–Carbowax–kieselguhr at 75° the fourth peak was partly resolved and showed two components. Separation of part (2·8 g.) by preparative-scale gas chromatography (column A, temp. 68°, N_2 flow rate 8·4 l./hr.) gave four fractions: (i) trifluoroethylene (trace); (ii) 1*H*,2*H*-hexafluorocyclobutane (III), b. p. 27° (0·6 g.); (iii) 1*H*,3*H*-hexafluorocyclobutane (XI) (1·0 g.); (iv) mixed fraction (1·2 g.). Fraction (iv) was shown to be 1*H*,2*H*-hexafluorocyclobutane (IV), b. p. 63°, and a new compound, in approximately equal

proportion; the last had additional infrared peaks at 1330, 1237, 1065, 1025, 885 and 834 cm.$^{-1}$ but none ascribable to −CF=CF− or −CF=CH− groups. Aliphatic hydrogen was present and the molecule appeared to be broadly similar to compound (IV).

Repetition of the experiment at 300—320° for 17 hr. gave the same products, from which 1H,3H-*hexafluorocyclobutane* (XI) (fraction ii) was isolated (yield *ca.* 15% on unrecovered olefin), with b. p. 38—39°, n_D^{25} 1·2850 (Found: C, 29·0; H, 1·2%), $\nu_{max.}$ 3009, 2974 cm.$^{-1}$ (>C−H). Mass spectrometry gave principal mass peaks 95 ($C_3H_2F_3$), 82 (C_2HF_3); the peak at 100 (C_2F_4) was virtually absent.

Dehydrofluorination of 1H,3H-*Hexafluorocyclobutane* (XI).—The compound (5·4 g.) and potassium hydroxide (20 g.) in water (15 c.c.) were stirred at 15°. After 5 min., spontaneous refluxing started. After 2½ hr., water (10 c.c.) was added, the mixture was cooled in an ice-bath, and the organic layer was separated quickly and dried, to give 3*H*-pentafluorocyclobutene (VI) (3·3 g.), b. p. 25—26°, having an infrared spectrum identical with that of the sample mentioned above.

Characterisation of 3H-*Pentafluorocyclobutene* (VI).—(a) *Bromine addition.* Compound (VI) (0·9 g.) and bromine (1·0 c.c.) were shaken for 2½ hr. in a sealed hard-glass tube which was irradiated with ultraviolet light. The product was washed with 10% sodium hydrogen carbonate solution, dried, and distilled, to give 3H-1,2-*dibromopentafluorocyclobutane* (0·95 g.), b. p. 114—115°/743 mm., n_D^{22} 1·4107 (Found: C, 15·9; H, 0·3; F, 30·7. $C_4HBr_2F_5$ requires C, 15·8; H, 0·3; F, 31·3%).

(b) *Oxidation.* A small tube containing compound (VI) (1·1 g.) was dropped into a flask containing potassium permanganate (1·32 g.) in dry acetone (200 c.c.), which was then shaken and cooled in running water for 5 min. The flask was shaken at 10—15° for 30 min., and water (200 c.c.) then added. Most of the acetone was distilled off and the residue acidified with sulphuric acid, treated with aqueous sodium hydrogen sulphite to remove the precipitate, and extracted exhaustively with ether. The extract was dried ($MgSO_4$), evaporated, and dissolved in a little ether; aniline in ether was added to give a precipitate (1·88 g.), m. p. 180—182° (decomp.). Recrystallisation from acetone–chloroform gave dianilinium trifluorosuccinate, m. p. 181—182° (decomp.) (Found: C, 53·3; H, 4·6%; equiv., 177. Calc. for $C_{16}H_{17}F_3N_2O_4$: C, 53·6; H, 4·8%; equiv., 179) [cited,[20] m. p. 181—186° (decomp.)].

3,3,4,4-*Tetrafluorocyclobutene* (VII).—A solution of hexafluorocyclobutene (16 g.) in dry diethyl ether (20 c.c.) at −78° was added during 5 min. to a stirred suspension of lithium aluminium hydride (4·5 g.) in diethyl ether (100 c.c.) at −78°. After 5 min. further water (20 c.c.) was added cautiously, followed by 12N-sulphuric acid (50 c.c.) and more water (100 c.c.). The ether layer and ethereal extracts of the aqueous phase were dried ($MgSO_4$) and fractionally distilled through a 3′ column packed with Dixon gauzes. The distillate had b. p. 34° and was ether; a residue (36 g.) which remained was separated by preparative-scale gas chromatography (column B, temp. 48°, N_2 flow rate 48 l./hr., 2 portions) to give ether, and 3,3,4,4-tetrafluorocyclobutene (4·65 g.), b. p. 53·9—54·8°/738 mm., n_D^{20} 1·3102 (Found: C, 38·2; H, 1·6; F, 59·9. Calc. for $C_4H_2F_4$: C, 38·1; H, 1·6; F, 60·3%), for which cited values [11] were b. p. 50·4—50·5°/634 mm., n_D^{20} 1·3114. In the infrared there were bands at 1565 (−CH=CH−, very weak) and 3111 cm.$^{-1}$ (>C−H, weak). Mass spectrometry gave principal mass peaks, 126 ($C_4H_2F_4$), 107 ($C_4H_2F_3$), 100 (C_2F_4), 76 ($C_2H_2F_2$), 26 (C_2H_2).

Characterisation of 3,3,4,4-*Tetrafluorocyclobutene* (VII).—(a) *Bromine addition.* Compound (VII) (2·5 g.) was treated for 8 hr. with bromine (5·8 g.), as for compound (VI), to give 3,4-dibromo-1,1,2,2-tetrafluorocyclobutane (4·0 g.), b. p. 114—115°/750 mm., n_D^{21} 1·4229 (Found: C, 16·9; H, 0·7; Br, 55·5; F, 26·4. Calc. for $C_4H_2Br_2F_4$: C, 16·8; H, 0·7; Br, 55·9; F, 26·6%), for which b. p. 63—64°/79 mm. and n_D^{20} 1·4220 have been cited.[11] (b) *Oxidation.* Compound (VII) (1·5 g.), potassium permanganate (10 g.), and water (50 c.c.) were heated at 80° for 14 hr. in a rocking autoclave. Isolation as usual gave tetrafluorosuccinic acid (45%), m. p. 114—118°, identified as its dianilinium (m. p. 220—222°) and di-*S*-benzylthiouronium salt (m. p. 190—191°); both had correct analyses.

The authors thank Professor M. Stacey, F.R.S., for his interest, Dr. D. H. Whiffen for the infrared spectroscopy, Dr. J. R. Majer for the mass spectrometry, and the Medical Research Council for a Fellowship (to G. F.).

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627. *Structure and Reactivity of the Oxyanions of Transition Metals. Part XI.* Ultraviolet Spectra of Monosubstituted Chromate Ions.*

By U. Kläning and M. C. R. Symons.

The preparation of dilute solutions of chromates, $RO{\cdot}CrO_3^-$, where R is alkyl, substituted alkyl, or acyl, is described, and their ultraviolet spectra are compared with those deduced from formation constants for these esters, together with spectra of aqueous-alcoholic solutions containing acid chromate in addition to the monoesters. Characteristic changes in the energy and intensity of the second band in the ultraviolet spectra as the group R is varied are correlated with σ^* values for these groups, and hence a qualitative interpretation of the spectra is offered.

Conversion of chromate (CrO_4^{2-}) of symmetry T_d into mono-derivatives ($X{\cdot}CrO_3^-$) of symmetry C_{3v} results in marked changes in the ultraviolet spectra, those for all $X{\cdot}CrO_3^-$ ions being qualitatively similar to each other, but characteristically different from that of chromate [1,2,3] (cf. Fig. 1).

The spectra of monochromate esters presented earlier were deduced indirectly from calculated equilibrium constants, and the spectra of solutions containing considerable amounts of acid chromate.[2] Such measurements have now been extended to other monoalkyl and monoacyl chromates; the calculated spectra are now compared with experimental spectra of solutions containing chromium exclusively as the monosubstituted chromate.

Our aim was to test the applicability of an orbital-level scheme proposed [3] to account for the spectra of XMO_3 molecules having C_{3v} symmetry.[3] Our interest in the nature of these transitions arises in part from the photo-sensitivity of monochromate esters.[4,5]

Experimental

Materials.—Water was redistilled from alkaline permanganate. Alcohols were dried before distillation: methanol with magnesium; ethanol, propanol, propan-2-ol, and t-butyl alcohol with calcium; and 1,3-dichloropropan-2-ol, ethylene chlorohydrin and methylcellosolve (2-methoxyethanol) with sodium carbonate. The water content of acetic acid was determined by Karl Fischer titration, and the water then removed by mixing the acid with the calculated amount of acetic anhydride and storing the whole for 72 hr. at room temperature. Other materials were Merck's "p. A." or "für Chromatographie." Ammonium dichromate was Merck's "puriss."

Spectra in Anhydrous Solvents.—The solutions listed in Table 1 were prepared by dissolving ammonium dichromate in the anhydrous solvent, the reaction $(NH_4)_2Cr_2O_7 + 2ROH \longrightarrow 2NH_4{\cdot}RCrO_4 + H_2O$ occurring. These solutions were diluted to give suitable optical densities and it was established that Beer's law held in the 2×10^{-3} to 10^{-4}M-region. This means that, in contrast with solutions of chromate in dilute aqueous acids, the concentration of dichromate is always small in this concentration range. Chromate concentrations were estimated spectrophotometrically after dilution with aqueous sodium hydroxide. The extinction coefficient at 373 mμ was taken as 4830, and it was established that under these conditions the esters were completely hydrolysed to sodium chromate.

Solutions in anhydrous unsubstituted alcohols were stable for several days at room temperature, as judged from their absorption spectra. For other solvents it was necessary to extrapolate to zero time of the spectrophotometric measurements because of slow decomposition, so that these results are less accurate.

Measurements were made with a Beckman DU spectrophotometer whose cell compartment

* Part X, *J.*, 1960, 973.

[1] Helmholz, Brennen, and Wolfsberg, *J. Chem. Phys.*, 1955, **23**, 853.
[2] Kläning, *Acta Chem. Scand.*, 1957, **11**, 1313; 1958, **12**, 576.
[3] Bailey, Carrington, Lott, and Symons, *J.*, 1960, 290.
[4] Kläning, *Acta Chem. Scand.*, 1958, **12**, 807; 1959, **13**, 2152.
[5] Kläning and Symons, *J.*, 1960, 977.

was thermostatically controlled at 25° ± 0·1°. The procedure for estimating esterification equilibria was as described previously.[3]

Results are given in Table 1, and typical spectra are shown in Fig. 1. Extinction coefficients are based on a molar extinction coefficient of 1530 for acid chromate at 350 mμ. To allow for overlap between the bands the following procedure was adopted: it was assumed

FIG. 1. *Ultraviolet spectra of* (a) CrO_4^{2-} *in* H_2O, (b) $Bu^tO{\cdot}CrO_3^-$ *in* Bu^tOH, (c) $Pr^iO{\cdot}CrO_3^-$ *in* Pr^iOH, (d) $MeO{\cdot}CrO_3^-$ *in* MeOH, (e) $HCrO_4^-$ *in* H_2O, *and* (f) $AcO{\cdot}CrO_3^-$ *in* AcOH.

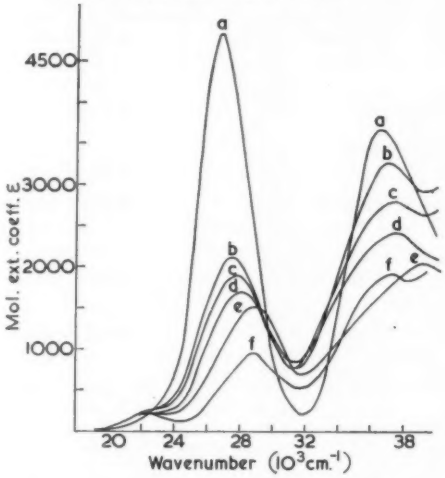


FIG. 2. *Correlation of the energies of maxima of the second band with their transition probabilities. (Key in Table* 1.)

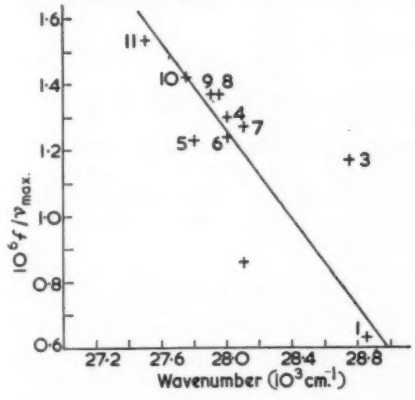


FIG. 3. *Correlation of transition probabilities for the second band with substituent constant* σ.* *(Key in Table* 1.)

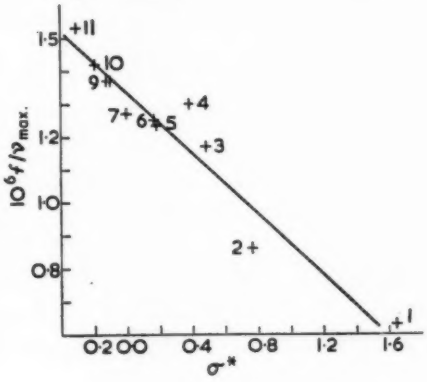
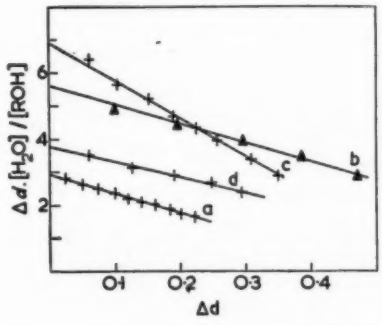


FIG. 4. *Plot of* $\Delta d[H_2O]/[ROH]$ *against* Δd *for potassium dichromate in aqueous solutions containing* (a) *ethylene chlorohydrin*, (b) *t-butanol*, (c) *ethylene glycol, and* (d) *acetic acid.*



that the first and the second band are symmetrical, that the third band contributes little at the peak of the second, that the first band has a maximum at 22,500 cm.$^{-1}$ in all cases, and that overlap of this with the second band does not extend below 22,000 cm.$^{-1}$. After subtraction of the first band, the maximum for the second was obtained by the method of mid-points, and the intensity was calculated by using the equation: $f = 4{\cdot}33 \times 10^{-9} \int \epsilon d\nu$. Unfortunately, resolution of the first band was such that subtle changes in this band would not have been observed.

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In Fig. 2 absorption maxima of the second bands are compared with their transition probabilities. The upward trend of the latter with decreasing energy is clear, although the

TABLE 1. *Ultraviolet spectra of mono-derivatives of chromates,* $RO{\cdot}CrO_3^-$ *in solvent* ROH.

$\nu_{max.}$ and $\varepsilon_{max.}$ are the band maxima ($cm.^{-1}$) and extinction coefficients derived from solutions of $(NH_4)_2Cr_2O_7$ in these solvents, $\nu_{max.}$ (calc.) and $\varepsilon_{max.}$ (calc.) those derived from K_E the equilibrium constant for $ROH + HCrO_4^- \rightleftharpoons RO{\cdot}CrO_3^- + H_2O$. f is the experimental oscillator strength for the first and second bands calculated from equation 1: σ^* is a measure of the electron-withdrawing power of R, taken from ref. 13.

No.	Solvent	$\nu_{max.}$	$\nu_{max.}$ (calc.)	10^2f	$10^6f/\nu_{max.}$	$\varepsilon_{max.}$	$\varepsilon_{max.}$ (calc.)	σ^*	K_E
1	AcOH	22,500		0·354	0·157	190		1·65	4·5
		28,850	28,900	1·82	0·633	945	810		
		37,300				1930			
2	$(CH_2Cl)_2CH{\cdot}OH$	22,500		0·353	0·157	200			
		28,100		2·41	0·857	1320		0·77 [a]	—
		—				—			
3	H_2O	22,500		0·352	0·157	200			
		28,750		3·37	1·17	1530		0·49	
		38,900				2060			
4	$CH_2Cl{\cdot}CH_2{\cdot}OH$	22,500		0·359	0·160	210		0·385	5·9
		28,000	28,000	3·64	1·30	1720	1770		
		37,200				2630			
5	$(CH_2{\cdot}OH)_2$	22,500		0·363	0·161	220			
		27,800	27,900	3·43	1·23	1760	1770	0·20	11·8
		37,000				2450			
6	$MeO{\cdot}CH_2{\cdot}CH_2{\cdot}OH$	22,500		0·376	0·167	220			
		28,000		3·59	1·24	1740		0·186	—
		37,200				2560			
7	MeOH	22,500		0·365	0·162	210			
		28,100	28,000	3·56	1·27	1700	1790	0·000	4·7
		37,400				2430			
8	EtOH	22,500		0·377	0·167	220			
		27,950	27,650	3·84	1·37	1820	1930	0·100	6·9
		37,250				2630			
9	Pr^nOH	22,500		0·406	0·180	225			
		27,900	27,650	3·82	1·37	1830	1930	0·115	9·7
		37,200				2600			
10	Pr^iOH	22,500		0·398	0·177	220			
		27,750	27,550	3·92	1·42	1910	2020	−0·190	8·3
		37,300				2810			
11	Bu^tOH	22,500		0·376	0·167	220			
		27,500	27,400	4·20	1·53	2120	2030	−0·300	5·8
		37,000				3280			

[a] Estimated by analogy from data for a series of related compounds given in ref. 13.

TABLE 2. *Isosbestic points* (mμ) *for* $(NH_4)_2Cr_2O_7$ *in aqueous alcohols.*

[ROH] (M)	Bu^t		Pr^iOH		[ROH] (M)	Bu^t		Pr^iOH	
2	318	338	321	341	8	316	341	321	342
4	318	340	323	341	100%	320	339	323	340
6	316	341	321	342					

results for acid chromate and 1,3-dichloropropan-2-ol are rather poorly correlated. Variation of the σ^* value for R,[6] with the transition probability is shown in Fig. 3: correlation with $\nu_{max.}$ is similar but a straight-line law is less well obeyed.

These results are self-consistent and thus support the view that monoesters $RO{\cdot}CrO_3^-$ are formed from the ammonium salt in anhydrous solvents: $Cr_2O_7^{2-} + 2ROH \longrightarrow 2RO{\cdot}CrO_3^- + H_2O$, and that little, if any $HCrO_4^-$ is present. Further support for this comes from the fact that good isosbestic points were found for the spectra of solutions prepared from ammonium dichromate, water, and various alcohols (see Table 2). It is unlikely that diesters $(RO)_2CrO_2$ were formed under these conditions, but their absence was confirmed by extracting the solutions with iso-octane.

Spectra in Aqueous Solvents.—Equilibria of the type, $ROH + HCrO_4^- \rightleftharpoons ROCrO_3^- + H_2O$, were studied spectrophotometrically, as described previously,[2] by measuring the difference,

[6] Taft in Newman's "Steric Effects in Organic Chemistry," Wiley and Sons, Inc., New York, 1956.

Δd, in optical density between that of aqueous acid chromate and that of the same concentration of Cr^{VI} in a given solvent mixture. By neglecting activity coefficients, the relation

$$\Delta d[H_2O]/[ROH] = \Delta\varepsilon \,.\, K_E l[Cr^{VI}] - K_E \Delta d \quad . \quad . \quad . \quad . \quad . \quad (1)$$

can be derived,[2] where Δd is the difference between the extinction coefficients of $HCrO_4^-$ and $RO{\cdot}CrO_3^-$ at the wavelength used. The optical length of the cell, l, was 10 cm., and the concentrations of water, alcohol, and total Cr^{VI} were in the regions 30—55M, 0—5M, and 10^{-4}M respectively. The results are shown in Fig. 4 as a plot of $\Delta d[H_2O]/[ROH]$ against $\Delta d.K_E$ was calculated from the slopes of these plots, and the results are given in Table 1.

From measurements of Δd at various wavelengths, absorption spectra of the monoesters $RO{\cdot}CrO_3^-$ were constructed. These were all closely similar to those shown in Fig. 1, confirming the postulate that these are pure spectra of the monoesters. Wavelengths at which Δd was zero are listed in Table 2.

Discussion

Electron-spin resonance studies of ions such as manganate (MnO_4^{2-}), hypomanganate (MnO_4^{3-}), and ferrate (FeO_4^{2-}) have established, apparently without ambiguity, that the first excited level for closed-shell ions such as chromate is doubly degenerate,[7] and hence that the first intense band can be described as $t_1 \longrightarrow e$.[8] The t_1 orbital is non-bonding on oxygen and the e orbital is π-antibonding, but is probably largely localised as the $d\gamma$-orbital of the central metal.[9]

On going from closed-shell MO_4 ions to XMO_3 the symmetry is lowered from T_d to C_{3v}, and the t_1 level is split into a doublet ($4e$) and a singlet (a_2).[1,8] The first excited level remains a doublet ($5e$), although its energy, relative to that in MO_4 may be altered. The a_2 level involves only non-bonding electrons on oxygen, whereas the $4e$ level involves, in addition, non-bonding electrons on X.

There are thus two allowed transitions in place of the $t_1 \longrightarrow e$ transition of MO_4, and our problem is to decide which of the transitions $a_2 \longrightarrow 5e$ and $4e \longrightarrow 5e$ lies lower.

In an earlier analysis[3] based on calculations of oscillator strengths similar to those of Ballhausen and Lier,[10] it was concluded that the relatively weak long-wavelength band corresponded to the $4e \longrightarrow 5e$ transition and the second stronger band to the $a_2 \longrightarrow 5e$ transition. The key relation, that

$$f \,.\, MO_3X = f \,.\, MO_4 \times \tfrac{1}{3} \times \frac{\nu^1}{\nu}$$

(where f is the oscillator strength and ν^1 and ν are the transition-energies for MO_3X and MO_4) required by this theory for the $a_2 \longrightarrow e$ transition, was in satisfactory agreement with experiment only if data for the second band were used.

However, the whole basis of these calculations is now thought to be in error [11] and we have therefore turned to other methods for making an assignment.

From a chemical viewpoint it seems reasonable to suggest that, provided the electron-affinity of X differs sufficiently from that of oxygen, one of the two bands should involve electron-transfer primarily from X and the other from oxygen. In that case we conclude that, for the esters described above, which have approximate C_{3v} symmetry in the chromophore, transitions from RO should require greater energy than those from oxygen and that only the former transitions should be markedly dependent on the electron-affinity of R, shifting to shorter wavelengths as the electron-affinity of R increases. A similar trend is expected for the transition from halogen in halogenochromate ions on going down the Periodic Table. Further, as the electron-affinity of R increases and the amount of π-bonding to the oxygen of the RO group decreases, so the oscillator strength for any

[7] Carrington, Ingram, Lott, Schonland, and Symons, *Proc. Roy. Soc.*, 1960, *A*, **254**, 101.
[8] Carrington and Symons, *J.*, 1960, 889.
[9] Schonland, *Proc. Roy. Soc.*, 1960, *A*, **254**, 111.
[10] Ballhausen and Lier, *J. Mol. Spectroscopy*, 1958, **2**, 342.
[11] Carrington and Schonland, *Mol. Phys.*, 1960, **3**, 331.

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charge-transfer transition from this group will decrease, tending to zero as the amount of π-bonding decreases.

All these properties are found for the second band. In Fig. 2 the trend to smaller transition probabilities with increase in energy is shown, and in Fig. 3 the relation between transition probability and the σ* values for the substituents is given. Since σ* is a measure of the inductive effect of these groups,[6] this shows that, as the electron-attracting power of R increases so the transition probability decreases; and the energy also increases regularly.

In contrast, the first band is relatively insensitive to changes in R, as would be expected, on our simple picture, for a transition from the oxide ligands. We conclude, therefore, that the first band is $a_2 \longrightarrow 5e$, and the second $4e \longrightarrow 5e$.

These qualitative arguments are only reasonable provided the alkyl-oxygen is sufficiently different from the remaining three oxygens to warrant clear-cut differentiation between transitions involving non-bonding electrons on alkyl-oxygen and those involving the remainder. However, one cannot so readily justify any such differentiation between the three remaining oxide ligands of the monoesters, and the four ligands of the parent ion. It therefore seems probable that the low-intensity band which is invariably found in the 22,000 cm.$^{-1}$ region for mono-derivatives of chromate arises from the very weak band found by Teltow [12] on the long-wavelength edge of the first intense bands in the spectra of crystals containing CrO_4^{2-} and MnO_4^-. This band is presumably the $^1T_1 \longleftarrow {}^1A_1$ component of the $t_1 \longrightarrow e$ transition of these ions, which is forbidden by the electric-dipole selection rules. In C_{3v} symmetry, the $a_2 \longrightarrow e$ transition is $^1E \longleftarrow {}^1A_1$, and the $e \longrightarrow e$ transition has as allowed components $^1A_1 \longleftarrow {}^1A_1$ and $^1E \longleftarrow {}^1A_1$. Detailed calculations by Carrington [13] suggest that the intensity of the first band in the spectra of mono-derivatives of chromates is derived by a process of "borrowing" from the second transition, since both transitions have $^1E \longleftarrow {}^1A_1$ components.

Thanks are offered to Dr. A. Carrington for helpful discussion.

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Department of Chemistry, The University, Leicester. [*Received, January 25th*, 1961.]

[12] Teltow, *Z. phys. Chem.*, 1938, *B*, **40**, 397; 1939, *B*, **43**, 198.
[13] Carrington, unpublished work.

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628. *Arsinophosphonium Salts.*

By J. M. F. Braddock and G. E. Coates.

Many tertiary phosphines, R'_3P, react with halogenoarsines, R_2AsX, forming salts, $[R'_3P{\cdot}AsR_2]^+X^-$. Triphenylphosphine does not react. Though analogous salts are formed by some nitrogen bases, conductimetric titration shows pyridine to be a much weaker donor than triethylphosphine or dimethylphenylphosphine, to iododimethylarsine. Methoxydimethyl- and dimethylphenoxy-arsine have been prepared.

Dimethylarsinophosphonium salts, from halogenodimethylarsines and tertiary phosphines, *e.g.*, $Me_2AsI + Et_3P \longrightarrow [Me_2As{\cdot}PEt_3]^+I^-$, have been mentioned in a note.[1] We now report the scope of this reaction and some properties of the products. While this work was in progress a related series of compounds, derived from chloramine and tertiary phosphines (*e.g.*, $[Ph_3P{\cdot}NH_2]^+Cl^-$), was described.[2]

The salts prepared during the present work are listed in the Table. They are insoluble in non-polar solvents such as benzene and hexane and often slightly soluble in weakly

[1] Coates and Livingstone, *Chem. and Ind.*, 1958, 1366.
[2] Sisler, Sarkis, Ahuja, Drago, and Smith, *J. Amer. Chem. Soc.*, 1959, **81**, 2982.

Arsine	Phosphine	Salt	M. p.	Found (%) C	Found (%) H	Formula	Required (%) C	Required (%) H
Me_2AsCl	PEt_3	$[Me_2As{\cdot}PEt_3]Cl$ [a]	73—75° [b]	37·3	8·2	$C_8H_{21}AsClP$	37·2	8·1
,,	$PPhMe_2$	$[Me_2As{\cdot}PPhMe_2]Cl$ [a]	115—116 [c]	43·6	6·2	$C_{10}H_{17}AsClP$	43·3	6·1
Me_2AsBr	PEt_3	$[Me_2As{\cdot}PEt_3]Br$	142—145 [d]	31·8	7·1	$C_8H_{21}AsBrP$	31·8	7·0
,,	$PPhMe_2$	$[Me_2As{\cdot}PPhMe_2]Br$	178 [d]	37·3	5·6	$C_{10}H_{17}AsBrP$	37·3	5·3
,,	$PPhEt_2$	$[Me_2As{\cdot}PPhEt_2]Br$	142—148 [c]	41·3	6·3	$C_{12}H_{21}AsBrP$	41·1	6·0
Me_2AsI	PMe_3	$[Me_2As{\cdot}PMe_3]I$	270—273 [f]	20·2	5·1	$C_5H_{15}AsIP$	19·6	4·9
,,	PEt_3	$[Me_2As{\cdot}PEt_3]I$ [a]	132—135 [d]	27·7	6·0	$C_8H_{21}AsIP$	27·6	6·0
,,	PPr^n_3	$[Me_2As{\cdot}PPr^n_3]I$	100 [c]	33·2	6·9	$C_{11}H_{27}AsIP$	33·7	6·9
,,	$PPhMe_2$	$[Me_2As{\cdot}PPhMe_2]I$ [a]	147 [d]	32·3	4·6	$C_{10}H_{17}AsIP$	32·4	4·6
,,	PPh_2Me	$[Me_2As{\cdot}PPh_2Me]I$	115—117 [d]	42·1	4·5	$C_{15}H_{19}AsIP$	41·7	4·4
Et_2AsI	$PPhMe_2$	$[Et_2As{\cdot}PPhMe_2]I$	112—118 [d]	36·4	5·5	$C_{12}H_{21}AsIP$	36·3	5·3
Ph_2AsI	PEt_3	$[Ph_2As{\cdot}PEt_3]I$	85—87 [d]	45·4	5·6	$C_{18}H_{25}AsIP$	45·4	5·3

[a] Previously described (ref. 1). [b] Crystallized from ethanol–ether, [c] from acetone, [d] from ethanol, [e] from propan-1-ol, [f] from ethanol–water.

polar solvents (ether or tetrahydrofuran), and can generally by crystallized from acetone, ethanol, or propanol. Of the salts studied only dimethylarsinotrimethylphosphonium iodide, $[Me_2As{\cdot}PMe_3]I$, was stable to air and water; the rest decomposed (sometimes rapidly) in air by hydrolysis and oxidation, but remained undecomposed when stored under nitrogen. Some of the iodides, for example the methyl compound just mentioned, can be sublimed in a vacuum, presumably by reversible dissociation like the ammonium and phosphonium halides.

Although the aminophosphonium halides [2] are hydrolysed to phosphine oxides:

$$R_3P{\cdot}NH_2^+ + OH^- \longrightarrow R_3PO + NH_3,$$

and phosphine oxides are also formed by attack of base on quaternary phosphonium salts: [3]

$$R_4P^+ + OR'^- \longrightarrow R_3PO$$

the arsinophosphonium salts are hydrolysed to the tertiary phosphine and the arsenoxide:

$$[R_2As{\cdot}PR'_3]^+ + OH^- \longrightarrow (R_2As)_2O + PR'_3$$

We attribute this to reversible dissociation of the arsinophosphonium salt,

$$R_2As{\cdot}PR'_3{}^+X^- \rightleftharpoons R_2AsX + PR'_3$$

which is apparent from conductimetric titrations (see below), followed by rapid hydrolysis of the halogenoarsine, $2R_2AsX + 2OH^- \longrightarrow (R_2As)_2O + 2X^- + H_2O$. Reactions with MeO^- and PhO^- anions again yield the tertiary phosphine, with methoxy- and phenoxydimethylarsine:

$$[Me_2As{\cdot}PEt_3]I + NaOMe \longrightarrow Me_2AsOMe + PEt_3 + NaI$$

Since no reference could be found to compounds $Me_2As{\cdot}OR$ (R = Me or Ph), both these very readily hydrolysed compounds were prepared from iododimethylarsine, *e.g.*:

$$Me_2AsI + NaOMe \longrightarrow Me_2As{\cdot}OMe$$

The apparent molecular weights of the salts $[Me_2As{\cdot}PEt_3]I$ and $[Me_2As{\cdot}PPr_3]I$, measured cryoscopically in nitrobenzene, were rather more than half the formula weights.

Conductances.—In nitrobenzene at 25° the molar conductances of the iodides $[Me_2As{\cdot}PEt_3]I$ and $[Me_2As{\cdot}PPhMe_2]I$ were practically linear functions of the square root of the molar concentration M, according to the equations $\Lambda = 35{\cdot}6 - 197M^{\frac{1}{2}}$ and $\Lambda = 30{\cdot}6 - 142M^{\frac{1}{2}}$, respectively. These values of Λ_0, 35·6 and 30·6, are appropriate for a 1 : 1 electrolyte in nitrobenzene.

Conductimetric titration (Fig. A) of triethylphosphine with iododimethylarsine shows a well-defined discontinuity close to the theoretical equivalence point. When dimethylphenylphosphine (Fig. B) or methyldiphenylphosphine (Fig. C) are titrated with iododimethylarsine, the equivalence point is not well marked (see particularly Fig. C). We

[3] Berlin and Butler, *Chem. Rev.*, 1960, **60**, 243.

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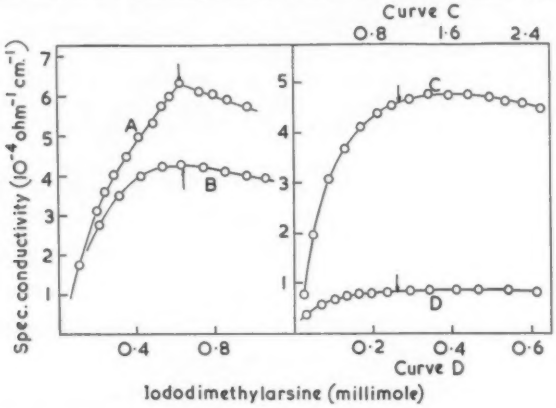
attribute these results to the reversibility of the reaction, and the diarylphosphine PPh_2Me is clearly a weaker donor to iododimethylarsine than is $PPhMe_2$ in the sense that the equilibrium, $Me_2AsI + PR_3 \rightleftharpoons Me_2As{\cdot}PR_3^+ + I^-$, lies further to the left. The titration with pyridine (Fig. D) shows that this base is considerably weaker still; in fact, the very unstable pyridinium salt $[C_5H_5N{\cdot}AsMe_2]I$ was difficult to isolate, could not be purified satisfactorily, and slowly decomposed into its components even when kept in a vacuum at room temperature. Towards iododimethylarsine the donor character of the bases studied is in the order: $PEt_3 > PPhMe_2 > PPh_2Me > C_5H_5N > PPh_3 = 0$.

Halogenodiphenylarsines do not react with tertiary phosphines as readily as the dialkylhalogenoarsines. Though the iodide $[Ph_2As{\cdot}PEt_3]I$ was the only diphenylarsino-derivative that could be isolated, its instability was shown by a marked curvature of the

Conductimetric titration of tertiary phosphines, (A) PEt_3, (B) $PPhMe_2$, *and* (C) PPh_2Me, *and of pyridine* (D) *with iododimethylarsine. Arrows indicate equivalence points.*



conductimetric plot in the vicinity of the end-point. Evidence for the formation of the chloride, which could not be isolated in a pure state, was obtained only from a conductimetric titration. Similarly, unstable salts were formed from triethylphosphine and iododiphenyl-antimony and -bismuth, but in neither instance could a pure product be isolated.

Co-ordination between phosphorus and arsenic occurs in the halide complexes described by Holmes,[4] *e.g.*, Me_3As,PCl_3, but in such a compound it is likely that arsenic is the donor.

Experimental

All the compounds were prepared under an inert atmosphere. The preparation of only one phosphonium salt is described since all the others were prepared by a very similar method.

Dimethylarsinodimethylphenylphosphonium Iodide.—Dimethylphenylphosphine (27·6 c.c., 0·2 mole) in ether (70 c.c.) was slowly (10 min.) added to a stirred solution of iododimethylarsine (33·2 c.c., 0·2 mole) in ether (250 c.c.). The *phosphonium salt* was precipitated in a rapid and exothermic reaction. After 2 hours' stirring the salt was separated and crystallized from ethanol (2 l.) as white square plates (48·5 g., 62%), m. p. 147° (see Table).

Dimethylarsinopyridinium Iodide.—Dry pyridine (8·0 g.) was added to iododimethylarsine (23 g.) in ether (50 c.c.). The ether was removed by evacuation for a few minutes at room temperature; the pale yellow solid residual *iodide* crystallised from ethanol as colourless leaflets, m. p. 194° (decomp.) (Found: C, 28·6; H, 3·3; I, 39·0. $C_7H_{11}AsIN$ requires C, 27·1; H, 3·5; I, 40·9%).

Methoxydimethylarsine.—Sodium methoxide (9·5 g.) and iododimethylarsine (18·5 g.) were

[4] Holmes, *J. Amer. Chem. Soc.*, 1960, **82**, 5285; *J. Phys. Chem.*, 1960, **64**, 1295.

boiled in xylene under reflux until the yellow colour of the iododimethylarsine had disappeared (4 hr.). Distillation followed by three fractional distillations (nitrogen atmosphere) yielded a colourless *arsine*, b. p. 79° (1·276 g., on hydrolysis and oxidation with hydrogen peroxide, gave 1·289 g. of dimethylarsinic acid. C_2H_9AsO requires 1·292 g.).

Dimethylphenoxyarsine.—Iododimethylarsine (18·5 g.) was added to sodium phenoxide (11·6 g., 0·1 mol.; excess of phenol had been removed by sublimation) in tetrahydrofuran (65 c.c.). A white solid was precipitated and the yellow colour of iododimethylarsine almost disappeared. The *phenoxyarsine* was isolated by distillation and had b. p. 204° (slight decomp.), 101°/12 mm. (Found: C, 49·5; H, 5·6. $C_8H_{11}AsO$ requires C, 48·5; H, 5·8%. 1·312 g. after hydrolysis and bromination gave 2·183 g. tribromophenol. $C_8H_{11}AsO$ requires 2·183 g.).

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629. *Condensed Ions in Aqueous Solutions. Part II.* Compounds of Quinquevalent Vanadium with Orthophosphate.*

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Phase studies of the system vanadium(v) oxide–phosphoric oxide–water at 25° with from 5% to 65% phosphoric oxide have shown the presence of two sparingly soluble yellow compounds $V_2O_5,P_2O_5,6H_2O$ and $V_2O_5,1{\cdot}5P_2O_5,6{\cdot}5H_2O$ as stable solid phases.

Ion-exchange and potentiometric titration studies of the red solutions obtained by adding phosphoric acid to solutions of vanadates have indicated a decavanadophosphate ion to be the only heteropolyanion formed.

EARLY studies [1-3] revealed two types of compounds containing quinquevalent vanadium and orthophosphate. In one series the ratio of vanadium to phosphate was low and the compounds were yellow, while in the other the ratio was high and the colour red. Modern views accord with those of Friedheim [3] who regarded the yellow compounds as containing basic (*i.e.*, cationic) vanadium and the red ones as containing acidic (anionic) vanadium (vanadophosphates).

Various yellow vanadyl(v) phosphates have been described and the ratios of vanadium to phosphate found have been 2 : 1, 3 : 2, 1 : 1, 2 : 3, and 1 : 2, of which the value 1 : 1 has been most frequently recorded.[4,5] In a study of the system vanadium(v) oxide–phosphoric oxide–water at 25°, Tietze [6] had difficulties in that metastable solid phases were found to separate, but he found evidence for compounds with vanadium to phosphate ratios of 1 : 1, 2 : 3, and 1 : 3. Of these the first two appear to be stable and the third metastable.

Solid vanadophosphates have been reported with the ratios of vanadium to phosphorus of 4 : 1,[1] 8 : 1,[7] 10 : 1,[8] 12 : 1,[3,5] and 20 : 1.[2] Jander and Jahr [7] observed that when phosphoric acid was added to vanadic acid the ion formed had approximately the same diffusion coefficient as the ion present in vanadic acid solutions. It was evident, however, that most of the knowledge of the nature of both the vanadyl phosphates and the phosphovanadates was based on the analytical data for solid materials precipitated under a wide

* Part I, *J.*, 1958, 4708.

[1] Ditte, *Compt. rend.*, 1886, **102**, 757, 1019, 1105.
[2] Gibbs, *Amer. Chem. J.*, 1885, **7**, 209.
[3] Freidheim and Szamatolsky, *Ber.*, 1890, **23**, 1530.
[4] Rosenheim and Yang, *Z. anorg. Chem.*, 1923, **129**, 181; Rosenheim, Brauer, and Materne, *ibid.*, 1934, **220**, 73; Jander, Jahr, and Witzmann, *ibid.*, 1934, **217**, 65.
[5] Souchay and Dubois, *Ann. Chim.* (*France*), 1948, **3**, 88.
[6] H. R. Tietze, M.Sc. Thesis, London, 1952.
[7] Jander and Jahr, *Kolloid-Beih.*, 1934, **41**, 1, 297.
[8] Rosenheim and Pieck, *Z. anorg. Chem.*, 1916, **98**, 223.

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variety of conditions. The present studies had as their object a more systematic study of both systems.

Experimental

Phase-diagram Studies.—Vanadic oxide was added in small portions to solutions of phosphoric acid with stirring until an undissolved residue remained. The solutions and solids were left in contact with intermittent stirring in stoppered tubes immersed in a thermostat-bath at 25° for three months, by which time no further changes in the compositions of the aqueous phases could be detected. The liquids and the moist solid phases were then separated by

Table 1. *The system* V_2O_5–P_2O_5–H_2O *at* 25°

Solution		Moist solid phase		Solution		Moist solid phase	
V_2O_5 (%)	P_2O_5 (%)	V_2O_5 (%)	P_2O_5 (%)	V_2O_5 (%)	P_2O_5 (%)	V_2O_5 (%)	P_2O_5 (%)
0·6	5·7	32·4	26·9	0·05	38·4	25·8	39·0
0·5	12·6	35·2	30·5	0·07	39·8	22·6	41·6
0·2	18·2	20·0	24·8	0·07	45·8	17·9	43·9
0·4	19·0	21·7	25·3	0·07	52·0	20·5	46·4
0·35	28·6	28·4	32·1	0·17	64·6	8·0	59·0
0·25	28·7	16·7	15·8	0·12	64·6	14·2	56·3
0·3	30·9	33·9	40·4				

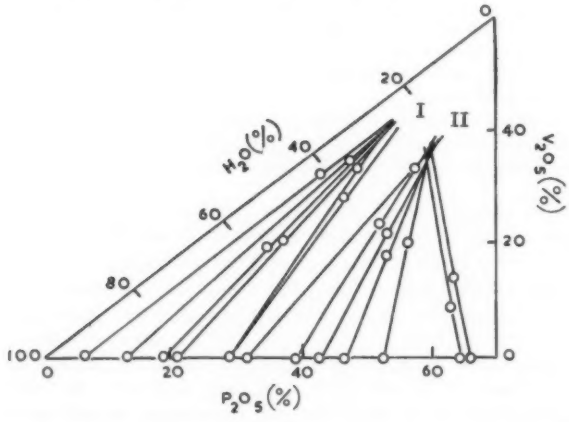

Fig. 1. *The system* V_2O_5–P_2O_5–H_2O *at* 25°.
I = V_2O_5,P_2O_5,$6H_2O$.
II = $2V_2O_5$,$3P_2O_5$,$13H_2O$.

filtration and aliquot parts or samples of each were analysed. The analytical data are given in Table 1 and in Fig. 1.

Ion-exchange Experiments.—(a) *Batch experiments.* Solutions (150 ml.) of known composition were left in contact with 0·5-g. portions of anion-exchanger (DeAcidite FF, Cl-form, water regain 1·82) for 150—200 hr. The solution was then separated from the resin, and aliquot portions were analysed. From the analytical data the R values [9,10] were calculated (see Table 2), namely:

$$R_v = \frac{\text{G.-atoms of V in solution initially} - \text{g.-atoms of V in solution finally}}{\text{G.-atoms of Cl in solution finally}}$$

and $$R_p = \frac{\text{G.-atoms of P in solution initially} - \text{g. atoms of P in solution finally}}{\text{G.-atoms of Cl in solution finally}}.$$

(b) *Column experiments.* Solutions (500 ml.) of known composition were passed during 3 days through a small column of anion exchanger (0·5 g. of DeAcidite FF, Cl-form, water regain 1·82), aliquot portions of the effluent were analysed, and R_v and R_p calculated (Table 2). The choice of a resin of water regain 1·82 was governed by the inference (drawn from Jander's

[9] Russell and Salmon, *J.*, 1958, 4708.
[10] Everest and Salmon, *J.*, 1954, 2348.

observation [7]) that the vanadophosphate ion was comparable in size with the decavanadate ion (see ref. 9).

Potentiometric Titration.—An aqueous solution of ammonium vanadate (0·068 g.-atom of V; pH 9·5) and one of ammonia (pH 9·5) were each titrated with phosphoric acid (0·5 mole), and the changes in pH during the titration followed by use of a glass electrode–calomel electrode system with a commercial pH-meter. If, at a given pH, P_x g.-atoms of phosphorus (as H_3PO_4) had been added to the ammonium vanadate solution and P_y g.-atoms of phosphorus to the ammonia

TABLE 2. *Anion-exchange experiments with vanadophosphate solution using DeAcidite* FF (0·5 g. *of* Cl-*form, water regain* 1·82).

	Initial solution					
	10^2 g.-atoms/l.			Vol. used		
Experiment	V	P[c]	pH	(ml.)	R_v	R_p
Column	6·5[a]	6·5	1·8	500	3·17[e]	0·33[e]
Batch	6·5[a]	6·5	1·8	150	3·29 (±0·03)	0·37 (±0·03)
,,	6·6[b]	*d*	1·8[d]	150	3·3	*g*
,,	6·6[b]	*d*	2·6[d]	150	3·4	*g*
,,	6·6[b]	*d*	2·9[d]	150	3·3	*g*
,,	6·6[b]	*d*	3·5[d]	150	3·0	*g*
,,	6·6[b]	*d*	4·0[d]	150	3·0	*g*
,,	6·6[b]	*d*	4·4[d]	150	2·9	*g*
,,	6·6[b]	*d*	4·9[d]	150	2·6	*g*
,,	6·6[b]	*d*	5·6[d]	150	2·6	*g*
,,	6·6[b]	*d*	5·9[d]	150	2·6	*g*
,,	7·4[b]	3·2	5·0—5·4	150	2·55 (±0·05)[f]	0·27 (±0·06)[f]
,,	7·4[b]	3·3	5·6—5·9	150	2·55 (±0·10)[f]	0·24 (±0·06)[f]

[a] As vanadic acid prepared from ammonium vanadate solution by passage through ZeoKarb 225 (H-form) column. [b] As ammonium vanadate. [c] Added as orthophosphoric acid. [d] pH varied by addition of varying amounts of phosphoric acid. [e] Mean of 4 experiments. [f] Mean of 3 experiments. [g] Not determined.

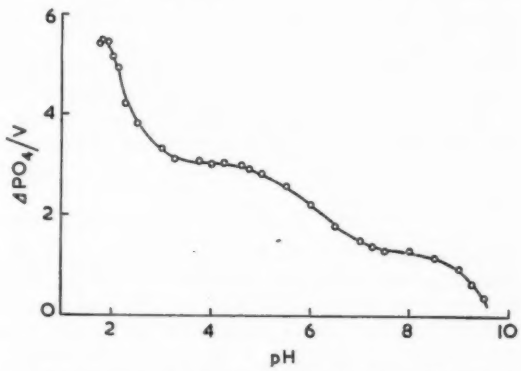

FIG. 2. *Titration of ammonium vanadate with phosphoric acid.*

solution, then it was found that $P_x \gg P_y$. It was assumed that P_x represented phosphoric acid used to neutralise the free ammonia arising by hydrolysis of the ammonium vanadate solution (P_z) and additional phosphoric acid to provide hydrogen ions used in a condensation reaction. A further assumption made was that $P_y = P_z$ and hence that $\Delta P = P_x - P_y$ represented the phosphoric acid used in the latter reaction. A plot of $\Delta PO_4/V$ (where $V = 0{\cdot}068$ g.-atom of vanadium) against pH is given in Fig. 2.

Analysis.—Vanadium and chloride were determined as previously described,[9] and phosphate gravimetrically as ammonium phosphomolybdate after removal of vanadium by reduction to vanadium(IV) and sorption of the latter on a column of ZeoKarb 225 cation-exchanger.[11]

RESULTS AND DISCUSSION

Vanadyl Phosphates.—Because of the very low solubility of the yellow vanadyl phosphates in phosphoric acid solution (Fig. 1, Table 1) it was impossible to discuss the break in

[11] Salmon and Tietze, *J.*, 1952, 2324.

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the solubility isotherm corresponding to the change in solid phase, but from the tie lines (Fig. 1) it is evident that a compound of composition $V_2O_5,P_2O_5,6H_2O$ (I) is the stable solid phase for solutions containing from 5% to ~30% phosphoric oxide and that from these to at least 65% phosphoric oxide the stable solid phase is $2V_2O_5,3P_2O_5,13H_2O$ (II). Compound (I) corresponds to $(VO)PO_4,3H_2O$ or to $(VO_2)H_2PO_4,2H_2O$, and compound (II) to $(VO)_2(HPO_4)_3,5H_2O$ or to $[(VO_2)H_2PO_4]_2,H_3PO_4,3H_2O$. The vanadyl(v) cation in solution appears to be $[VO_2]^+$ (ref. 12), and this is in accord with its very low relative affinity (as compared with hydrogen ions) for a cation-exchanger. Nevertheless, formulation of the solid compounds as derivatives of the VO^{3+} cation is preferred for three reasons: (i) the low solubility of the compounds in phosphoric acid is typical of tervalent phosphates [*e.g.*, Fe(III), Bi(III)] rather than of univalent ones; (ii) in no case so far studied (see, *e.g.*, ref. 13) has a primary (*i.e.*, dihydrogen) phosphate appeared as solid phase in contact with solutions containing less than 30% phosphoric oxide; and (iii) all compounds containing "phosphoric acid of crystallisation," such as $[(VO_2)H_2PO_4]_2,H_3PO_4,H_2O$ are readily soluble, deliquescent compounds (see, *e.g.*, ref. 13*a*) whereas compound II is highly insoluble.

In view of the very low solubility of the compounds no attempt was made to study their state in solution.

Vanadophosphates.—The results of the ion-exchange experiments with the red vanadophosphate solutions (Table 2) are consistent with the sorption of $[HPV_{10}O_{30}]^{4-}$ ions ($R_v = 2{\cdot}5$, $R_p = 0{\cdot}25$) over the pH range 4·9—5·9, of $[H_2PV_{10}O_{30}]^{3-}$ ions ($R_v = 3{\cdot}3$, $R_p = 0{\cdot}33$) over the pH range 1·8—2·9, and of a mixture of these between pH 2·9 and 4·9. There seems to be little competition from isopolyvanadic ions or from phosphate ions. Since in all the solutions studied the amount of phosphate present exceeds by at least four-fold that required to form decavanadophosphate ions the concentration of isopolyvanadate is probably low. Although some bivalent HPO_4^{2-} ions must be present in the solution of pH >5 the proportion of these is probably insufficient to complete effectively with the decavanadophosphate which presumably is like the decavanadate ion in being very strongly sorbed. Results for solutions of pH >6 were variable and inconsistent.

The plot of $\Delta P/V$ against pH (Fig. 2) shows two inflexions, at about $\Delta P/V = 1{\cdot}3$ and 3·0, which would correspond respectively to the reactions:

$$10VO_4^{3-} + 14H_3PO_4 = [HPV_{10}O_{30}]^{4-} + 14H_2O + 13HPO_4^{2-} \quad (\Delta P/V = 1{\cdot}4)$$

and

$$10VO_4^{3-} + 27H_3PO_4 = [HPV_{10}O_{30}]^{4-} + 14H_2O + 26H_2PO_4^{-} \quad (\Delta P/V = 2{\cdot}7)$$

It may be noted that the first inflexion occurs at pH 7—8, at which the phosphate ions are present mainly as HPO_4^{2-} ions, and the second at pH 4·6 at which the phosphate ions will be present mainly as $H_2PO_4^-$ ions. The fact that the experimental value of $\Delta P/V$ (3·0) is slightly greater than that calculated (2·7) may arise from incomplete dissociation of the phosphoric acid to $H_2PO_4^-$. If this is accepted then the value of $\Delta P/V = 3{\cdot}3$ at pH 3 is in reasonable accord with the reaction:

$$10VO_4^{3-} + 28H_3PO_4 = H_3PV_{10}O_{30}^{3-} + 14H_2O + 27H_2PO_4^- \quad (\Delta P/V = 2{\cdot}8)$$

since at this pH the first dissociation of the phosphoric acid will be still less complete. Thus the results of both ion-exchange and potentiometric studies can be explained in terms of a decavanadophosphate ion which is $[H_2PV_{10}O_{30}]^{3-}$ at pH 1·8 and $[HPV_{10}O_{30}]^{4-}$ at pH ~6 (and this possibly present in diminishing amount up to pH 8.

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[12] Carpenter, *J. Amer. Chem. Soc.*, 1934, **56**, 1847.
[13] (*a*) Salmon and Terrey, *J.*, 1950, 2813; (*b*) Jameson and Salmon, *J.*, 1954, 28, 4013; 1955, 360; (*c*) Redfern and Salmon, *J.*, 1961, 291.

630. *The Preparation and Properties of Some Tetrakis(methyl cyanide)copper(I) Complexes.*

By B. J. Hathaway, D. G. Holah, and (in part) J. D. Postlethwaite.

The use of metallic copper as a reducing agent is described for the preparation of tetrakis(methyl cyanide) complexes of cuprous tetrafluoroborate, perchlorate, and nitrate. Some properties (molecular weights, conductivities, differential thermal and thermogravimetric analysis and infrared spectra) of the complexes are reported.

After the studies of the reaction between nitrosyl perchlorate and metallic copper in methyl cyanide,[1] where no trace of cuprous species was found, the analogous reaction with nitrosyl tetrafluoroborate has been investigated.[2] In this, a mixture of cuprous and cupric tetrafluoroborate complexes was obtained. The cuprous complex is formed by reduction of the cupric complex by metallic copper, which was first used as a reducing agent by Morgan [3] for the preparation of cuprous chloride– or bromide–mono(methyl cyanide) complexes. This reducing property of copper has now been extended to the preparation of other cuprous complexes.

Experimental

Preparation of Nitrosyl Tetrafluoroborate.[4]—Equivalent amounts of dinitrogen tetroxide and 70—80% fluoroboric acid were mixed at 0° and the precipitate of nitrosyl tetrafluoroborate purified by sublimation under a vacuum at 220°.

Reaction of Copper with Suspensions of Nitrosyl Tetrafluoroborate in Methyl Cyanide.—Powdered nitrosyl tetrafluoroborate (1 g.) was washed with dry ethyl acetate and transferred to a 250 ml. flask closed by a phosphorus pentoxide guard tube. A piece of clean copper sheet (30 × 10 × 1 mm.) and dry methyl cyanide (30 ml.) were added quickly. The flask was immediately evacuated through the guard tube by means of a water pump.[1] Reaction continued with rapid evolution of nitric oxide for about 3 hr., after which the solution was blue-green. The solution was filtered through a No. 4 sintered-glass filter-stick to remove traces of copper and the excess of nitrosyl tetrafluoroborate.

Quantitative tests showed that this solution contained both cuprous and cupric copper. The initial product, cupric tetrafluoroborate, formed by the reaction $2NO^+ + Cu^0 \longrightarrow Cu^{2+} + 2NO$, is partially reduced to cuprous tetrafluoroborate by the copper metal present: $Cu^0 + Cu^{2+} = 2Cu^+$. The latter reaction suggests a useful route to cuprous salts from the corresponding cupric salts, especially as the reduction goes to completion on refluxing.

Preparation of Cuprous Complexes.—The above solution (or one of cupric perchlorate [1] or nitrate in methyl cyanide) was refluxed with copper powder until the solution became colourless. The hot solution was filtered and the cuprous complex which crystallised on cooling was filtered off and dried in a vacuum. The nitrate complex is much less stable than the tetrafluoroborate or perchlorate complex and must be dried in a vacuum for not more than 1 min. if decomposition is to be avoided.

Electrolytic Reduction.—The preparation of the cuprous nitrate complex by electrolysis of cadmium nitrate in methyl cyanide solution at copper electrodes has been reported.[3]

When solutions of cupric tetrafluoroborate or perchlorate were electrolysed with a copper anode and either a copper or platinum cathode, the respective cuprous complexes were formed at the anode, while copper was deposited on the cathode. The cuprous nitrate solvate cannot be prepared by the electrolysis of cupric nitrate in methyl cyanide, since this solution is virtually non-conducting.[5]

Analysis of Solids.—Copper was estimated gravimetrically as copper ethylenediamine mercuri-iodide [6] after oxidation with nitric acid, and the anions as their nitron salts.

[1] Hathaway and Underhill, *J.*, 1960, 3705.
[2] Hathaway, Holah, and Underhill, unpublished work.
[3] Morgan, *J.*, 1923, 2901.
[4] Grunther, Balz, Erich, and Mailander, *Z. anorg. Chem.*, 1934, **217**, 161.
[5] Addison, Hathaway, Logan, and Walker, *J.*, 1960, 4308.
[6] Vogel, "Text Book and Quantitative Inorganic Analysis," Longmans, Green and Co., London, 2nd edn., 1951, p. 433.

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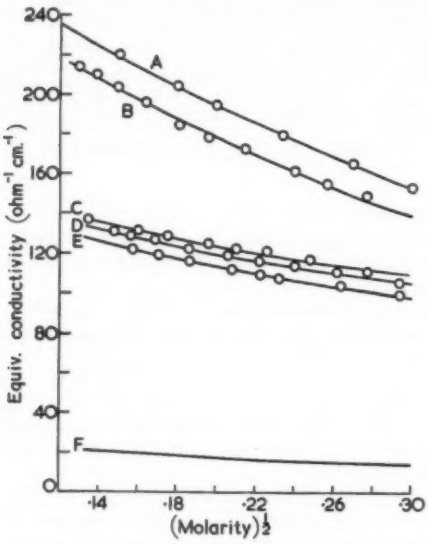
Analysis gave the following results. *Cuprous tetrafluoroborate complex*: Cu, 20·2; BF_4, 26·35% ($CuBF_4$,4MeCN requires Cu, 20·2; BF_4 27·6%). *Cuprous perchlorate complex*: Cu, 19·3; ClO_4, 29·6% ($CuClO_4$,4MeCN requires Cu, 19·45; ClO_4, 30·4%). *Cuprous nitrate complex*: Cu, 21·9; NO_3, 22·0% ($CuNO_3$,4MeCN requires Cu, 21·9; NO_3, 21·4%).

Properties of the Cuprous Complexes.—Appearance and melting points. The tetrafluoroborate and perchlorate solvates, m. p. 159—161° and 164—166° respectively, are white crystalline materials which decompose slowly in moist air. The white crystalline nitrate has m. p. 79—81° but decomposes almost immediately in air.

Apparent molecular weights. These were measured ebullioscopically with an apparatus of the Cottrell pump type,[7] methyl cyanide (20 ml.) being the solvent. The pellets were prepared in a small pellet-press in a dry box, and added at intervals down the condenser, closed at other



Equivalent conductivities in methyl cyanide solution.

A, $Cu(ClO_4)_2$. B, $Cu(BF_4)_2$. C, $Cu(MeCN)_4BF_4$. D, $Cu(MeCN)_4ClO_4$. E, $Cu(MeCN)_4NO_3$. F, $Cu(NO_3)_2$.

times by a loosely stoppered calcium chloride guard-tube. The temperatures were read through a small telescope (±0·002°). The apparatus was calibrated on Hopkin and Williams's naphthalene (" for molecular-weight measurements "). The variation in the apparent molecular weights of the complexes with concentration is shown in Table 1. The slight increase

TABLE 1. *Apparent molecular weights in methyl cyanide.*

$CuBF_4$,4MeCN				$CuClO_4$,4MeCN				$CuNO_3$,4MeCN			
Mol. wt.	Molarity	Mol. wt.	Molarity	Mol. wt.	Molarity	Mol. wt.	Molarity	Mol. wt.	Molarity	Mol. wt.	Molarity
70	0·026	77	0·063	79	0·037	84	0·073	73	0·037	74	0·089
72	0·036	78	0·072	82	0·047	84	0·080	72	0·050	74	0·099
73	0·045	77	0·098	84	0·056	86	0·100	72	0·061	77	0·119
76	0·052	78	0·119	84	0·065	86	0·111	72	0·079	78	0·131

in the apparent molecular weight of cuprous nitrate may be due to the presence of decomposition products since, when the methyl cyanide solution was cooled after the experiment, a small quantity of amorphous impurity settled out.

Over the concentration range studied the apparent molecular weights indicate that all the compounds are completely dissociated: $CuX \longrightarrow Cu^+ + X^-$. The values for cuprous nitrate are in complete contrast to the molecular weights of cupric nitrate in methyl cyanide,[5] which has been shown to be monomeric over this concentration range.

Molecular conductivities in methyl cyanide. These were measured by using a Cambridge

[7] Cottrell, *J. Amer. Chem. Soc.*, 1919, **41**, 721.

conductivity apparatus involving a 1000 cycles/sec. oscillator and a galvanometer as a null point instrument. The cell design was that of Groenevald and Zuuv,[8] which enables measurements to be made on hygroscopic solutions under a dry atmosphere.

The variations of molar conductivities with square root of molar concentrations are shown in Fig. 1. The conductivities of the three cuprous compounds are very close, all indicating complete dissociation of a 1 : 1 electrolyte, and agreeing with the molecular weights. The normal Onsager type equation is obeyed, although the plot of Λ against $\sqrt{c}$ is not exactly linear.

These values are compared with those obtained for cupric tetrafluoroborate[2] and perchlorate,[1] both of which show conductivities typical of a 2 : 1 electrolyte. The conductivity of cuprous nitrite is similar, but differs from that of the cupric compound which has a very low conductivity.[5]

Differential thermal analysis. The sample (0·1 g.) was contained in a small ignition tube into which dipped one terminal of a thermocouple, packed in position with glass wool. The other terminal was placed in a similar ignition tube containing powdered silica. Both the small tubes and a thermometer were contained in a B.24 tube placed in a vertical electric furnace. The thermocouple terminals were connected to a millivoltmeter, and the furnace current adjusted manually to give a heating rate of 3°/min. When the observed e.m.f. was recorded against the temperature, the cuprous tetrafluoroborate solvate showed only an endothermic peak, at 168°, corresponding to the m. p., indicating that endothermic decomposition probably occurs at the m. p. The perchlorate solvate showed clearly the endothermic m. p. at 175°, followed by explosive decomposition at 205°. A weak endothermic peak corresponding to the m. p. of the nitrate occurred at 95° and a weak endothermic peak at 138° is probably due to partial decomposition of the nitrate. Exothermic decomposition occurred at 141° owing to oxidation of methyl cyanide by nitrate ion, but the origin of a weak exothermic peak at 220° is unknown.

TABLE 2. *Infrared absorption frequencies* (cm.$^{-1}$).

$CuNO_3$,4MeCN	$Cu(NO_3)_2$	$CuBF_4$,4MeCN	KBF_4	$CuClO_4$,4MeCN	$KClO_4$
771w	770s	777w	773vw	779w	
	787s, b	789m, sp			
	795s, sh				
798m, sp					
815vw					
833vw					
	907w				
				925, 945 w, sh	927vw
1022m, sp	1016m, sh	1032, 1125 vs, b	1038, 1128 vs, b	1090, 1150 vs, b	1110vs, b
1040m, sh	1038s, b				
1168w					
1300vs, sp	1264vs, b	1290w		1310vw	
	1289vs, sh				
1345m	1344vs		1312vw		
	1504m, sp		1330vw	1370w	
	1546vs	1600vw	1623, 1671 vw		
	1565vs				2050w
	1592vs, sp				
2270, 2290 split		2270, 2290 split		2275, 2300 split	

The perchlorate solvate showed clearly the endothermic m. p. at 175°, followed by explosive decomposition at 205°. A weak endothermic peak corresponding to the m. p. of the nitrate occurred at 95° and a weak endothermic peak at 138° is probably due to partial decomposition of the nitrate. Exothermic decomposition occurred at 141° owing to oxidation of methyl cyanide by nitrate ion, but the origin of a weak exothermic peak at 220° is unknown.

Thermogravimetric analyses. These were carried out on a Stanton thermo-recording balance at a heating rate of 2°/min. The sample was contained in a small tube and an atmosphere of dry nitrogen maintained in the furnace. The weight loss (%) was recorded against temperature. Thermogravimetric analyses were carried out on the nitrate and tetrafluoroborate complexes, but not on the perchlorate because of its thermal instability.

With both complexes there is a gradual loss of methyl cyanide, followed by a much more rapid loss when anion oxidation of the methyl cyanide occurs. In neither case was any evidence for a stable intermediate obtained. Decomposition of the nitrate was complete by 160° and of the tetrafluoroborate by 270°, emphasising the lower thermal stability of the former. The

[8] Groenveld and Zuuv, *Rec. Trav. chim.*, 1953, **72**, 618.

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decomposition temperatures agree fairly well with the data from the differential thermal analysis. The total weight loss of the nitrate was 75·2% (decomposition to cupric oxide requires 72·5%) and for the tetrafluoroborate was 75·6% (decomposition to cupric oxide requires 74·7% and to cupric fluoride requires 67·8%).

These results show that the anhydrous cuprous salts cannot be prepared from their complexes, Even the use of low-temperature decomposition under a vacuum in the case of the nitrate failed to yield a compound of definite composition.

Infrared spectra. The spectra were determined for Nujol mulls in a Unicam S.P. 100 spectrophotometer. The main infrared absorption frequencies of the cuprous complexes are given in Table 2. The spectra of the tetrafluoroborate and perchlorate complexes are very similar to those of an ionic tetrafluoroborate [9] and perchlorate.[10] This evidence for the ionic nature of the complexes is consistent with molecular weights and molar conductivities in solution. The spectrum of the cuprous nitrate complex is very similar to that of cupric nitrate [11] which has been shown to contain nitrato-groups, and this strongly suggests that the solid complex also contains this group. The behaviour in methyl cyanide solutions, however, indicates complete dissociation to cuprous and nitrate ions, so the co-ordination is much weaker than in cupric nitrate.

The split absorptions at 2270—2300 cm.$^{-1}$ in the complexes are due to the $-C\equiv N$ vibration, which is shifted to slightly higher frequencies than the normal one at 2248 cm.$^{-1}$ in methyl cyanide. This is consistent with co-ordination of methyl cyanide to copper,[12] but does not distinguish between the strength of co-ordination of the tetrafluoroborate and perchlorate complexes and the less stable nitrate.

Discussion

The empirical formulæ of the complexes suggest that the cuprous ions are four co-ordinated, with the four molecules of methyl cyanide probably occupying the stereochemically preferred tetrahedral positions.[13,14] In solution there is no evidence to indicate that the cation is other than the tetrahedral tetrakis(methyl cyanide)copper(I), and a simple tetrafluoroborate, perchlorate, or nitrate anion. Although the solution properties are very similar, the very low thermal stability of the nitrate complex must be explained.

The nitrate ion as well as being smaller, is a flat trigonal ion as opposed to the essentially spherical tetrafluoroborate and perchlorate ions.[15] It also has a greater tendency to co-ordinate than the other two.[11,16] In the solid complex the nitrate ion may therefore approach (between two of the tetrahedrally co-ordinated methyl cyanide molecules) sufficiently close to the cuprous ion to form a weak copper to nitrate bond. This accounts for the infrared spectra; further, the close approach of the nitrate ion may distort the tetrahedral distribution of the methyl cyanide molecules, leading to the observed instability.

The authors are indebted to Dr. G. W. Gray for the infrared measurements, to the Chemical Society for a grant for apparatus, and to the Department of Scientific and Industrial Research for a maintenance grant (to D. G. H.).

The University, Hull. [*Received, February 22nd,* 1961.]

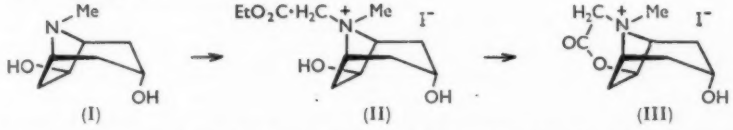
[9] Greenwood, *J.*, 1959, 3811.
[10] Miller and Wilkins, *Analyt. Chem.*, 1952, **24**, 1253.
[11] Addison and Gatehouse, *J.*, 1960, 613.
[12] Coerver and Curran, *J. Amer. Chem. Soc.*, 1958, **80**, 3522.
[13] Mann, Purdie, and Wells, *J.*, 1936, 1503.
[14] Cotton and Goodgame, *J.*, 1960, 5267.
[15] Bowen, Donohue, Jenkin, Kenward, Wheatley, and Whiffen, *Chem. Soc. Special Publ.* No. 11, 1958.
[16] Gatehouse, Livingstone, and Nyholm, *J.*, 1957, 4222.

631. *The Stereochemistry of the Tropane Alkaloids. Part XIII.* The Absolute Configuration and a Simplified Syntheses of Valeroidine.*

By Gábor Fodor, Irene W. Vincze, and Joseph Tóth.

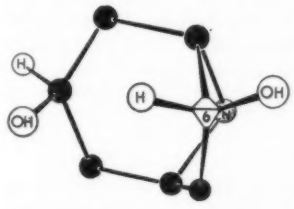
The configuration (3*R*,6*R*) has been assigned to natural valeroidine in view of the considerable dextrorotatory shift during lactonization of N_b-ethoxycarbonylmethyl-3α,6β-dihydroxytropanium iodide. Selective hydrolysis of tropane-3α,6β-diol di-isovalerate, leading to natural valeroidine, is described.

The relative configurations of the tropane alkaloids,[1] and the absolute configurations of the majority of them, *e.g.*, of cocaine,[2] hyoscyamine, and hyoscine,[3] have been determined recently. In a preliminary report [4] we assigned the (3*R*,6*R*) absolute configuration to valeroidine by adapting Hudson's lactone rule [5] to the cyclisation of N_b-ethoxycarbonylmethyl-3α,6β-dihydroxytropanium iodide [6] (II) to the six-membered lactone (III). We give now full details of the preparative work involved and of a simpler synthesis of natural valeroidine than reported heretofore.[7]



(I) (II) (III)

The lævorotatory form of the alkamine of natural valeroidine has been prepared both by the Stoll method [8] by resolving 6β-hydroxytropan-3-one with 3-bromo-(+)-camphor-7-sulphonic acid, and by resolving tropane-3α,6β-diol [9] with dibenzoyltartaric acid or 6β-phenylcarbamoyloxytropan-3α-ol [7] with (+)-tartaric acid. Since this lævorotatory alkamine has been converted into the same di-isovalerate [8] as was obtained by acylating tropane-3α,6β-diol, and since (+)-tropane-3α,6β-diol 6-phenylurethane has been converted stereospecifically into natural valeroidine,[7] configurational identity of (−)-valeroidine with (−)-tropane-3α,6β-diol was proved. Accordingly, extension of the conclusions reached with the alkamine to the natural alkaloid is justified. In consequence, (−)-tropane-3α,6β-diol (I) was treated with ethyl iodoacetate, giving as a first product the iodide of the lactone of N_b-carboxymethyl-3α,6β-dihydroxytropanium iodide. This proved to be strongly dextrorotatory. From the mother-liquor the ester, N_b-ethoxycarbonylmethyl-3α-dihydroxytropanium iodide (II), was obtained with a specific rotation of −23·7°. The latter compound showed m. p. 154° but resolidified, owing to lactonization, on further heating, and decomposed completely at 262°. On recrystallization from ethanol the ester was converted into the lactone.[6] A further correlation of the lactone and ester has been furnished by converting both compounds into the same betaine of m. p. 298—300°. The betaine proved to be strongly lævorotatory,



* Part XII, Dobó, Fodor, Janzsó, Koczor, Tóth, and Vincze, *J.*, 1959, 3461.

[1] Fodor, *Experientia*, 1955, **11**, 129; Fodor and his co-workers, *J.*, 1953, 721, 724, 2341; *Helv. Chim. Acta*, 1954, **37**, 892, 907.
[2] Hardegger and Ott, *Helv. Chim. Acta*, 1955, **38**, 312.
[3] Fodor and Csepreghy, *Tetrahedron Letters*, 1959, No. 7, 16.
[4] Fodor, Vincze, and Tóth, *Experientia*, 1957, **13**, 183.
[5] Hudson, *J. Amer. Chem. Soc.*, 1910, **32**, 338.
[6] Fodor, Tóth, and Vincze, *J.*, 1955, 3504.
[7] Fodor, Vincze, and Tóth, *J.*, 1957, 1349.
[8] Stoll, Lindenmann, and Jucker, *Helv. Chim. Acta*, 1953, **36**, 1506.
[9] Fodor and Kovács, *J.*, 1953, 2341.

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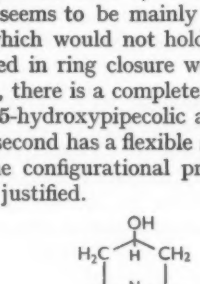
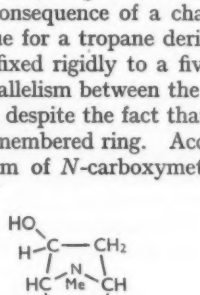
independently of the starting material. The betaine was reconverted into the lactone by evaporation of its aqueous solution with hydriodic acid. The strongly lævorotatory ester and betaine both gave the strongly dextrorotatory lactone (III) on acid treatment. According to Hudson's rule,[5] which has been applied recently by Witkop [10] to γ- and δ-hydroxyamino-acids, *e.g.*, both to γ-hydroxy-L-lysine and to 5-hydroxypipecolic acid, it seems justified to assign the D_g-configuration (Fig. 1 †) at position 6 and the overall (3*R*,6*R*) configuration (see IV and V) to the 3α,6β-tropanediol related to valeroidine. The change of rotation seems to be mainly a consequence of a change in conformation during lactonization, which would not hold true for a tropane derivative in which both the substituents involved in ring closure were fixed rigidly to a five-membered strained ring system. However, there is a complete parallelism between the optical changes of γ-hydroxy-L-proline and 5-hydroxypipecolic acid, despite the fact that the first has a rigid ring system whilst the second has a flexible six-membered ring. Accordingly, application of Hudson's rule to the configurational problem of *N*-carboxymethyl-3α,6β-dihydroxytropanium iodide seems justified.



(IV)



(V)

Decisive evidence would be obtained by converting either a compound of known absolute configuration into (−)-tropane-3α,6β-diol or, conversely, by degrading tropane-3α,6β-diol to a compound of known absolute configuration. Unfortunately, we have not succeeded as yet in effecting the latter transformation. However, an attempt is being made to correlate values on a sounder basis than the purely empirical with absolute configurations and conformations.[11] In the laboratory of one of the authors (G. F.) application of these Brewster principles is already in progress.

The roundabout way which had to be used to realize for the first time the total synthesis of valeroidine by thermal decomposition of (−)-6β-phenylcarbamoyloxytropan-3α-ol [7] was due to the failure of other authors [8] to perform selective hydrolysis of the corresponding diol divalerate. We found recently that use of a certain concentration of aqueous sodium hydroxide in acetone led to 3α-acetoxytropan-6β-ol in very good yield from the diacetyl derivative. This method proved generally applicable to other tropane-3α,6β-diol diesters, *e.g.*, both to (±)- and to (+)-3α,6β-di-isovaleryloxytropane. In this way the racemic di-isovalerate gave a 40% yield of pure racemic valeroidine hydrochloride, and (+)-3α,6β-di-isovaleryloxytropane gave a 30% yield of natural (−)-valeroidine.

Experimental

(+)-*Lactone of* N_b-*Carboxymethyl*-3α,6β-*dihydroxytropanium Iodide and* (−)-N_b-*Ethoxycarbonylmethyl*-3α,6β-*dihydroxytropanium Iodide*.—(−)-Tropane-3α,6β-diol (0·5 g.) was dissolved in a mixture of dry ethanol (5 ml.) and benzene (7 ml.). Ethyl iodoacetate (0·75 ml.) was added and the mixture refluxed for 10 hr. After 10 min. crystallization set in. The filtered crystals of *lactone iodide* (0·4558 g.) were extracted with boiling alcohol, then having m. p. 264° (decomp.), $[\alpha]_D^{30}$ +37·5° (*c* 2 in water) (Found: C, 37·4; H, 5·3; N, 4·3; I, 38·9. $C_{10}H_{16}INO_3$ requires C, 36·9; H, 5·0; N, 4·3; I, 39·0%). The mother-liquor and the alcohol used for extraction were evaporated; the residual *ester iodide* solidified on trituration with acetone. Recrystallized from alcohol–ether it (0·4031 g.) had m. p. 154°, with resolidification and decomposition at 262°, $[\alpha]_D^{30}$ −23·7° (*c* 1 in anhydrous ethanol) (Found: C, 38·6; H, 6·2; N, 3·6;

† To derive this configuration the projection is set up, as in Fig. 1, with C-1 at the top, C-6 in the middle, and C-5 at the bottom.

[10] Witkop, *Experientia*, 1957, **12**, 372.
[11] Brewster, *J. Amer. Chem. Soc.*, 1959, **81**, 5475, 5483.

I, 34·85. $C_{12}H_{22}INO_4$ requires C, 38·9; H, 5·9; N, 3·8; I, 34·25%). The total yield was 88·7%, calculated on starting material.

(−)-N_b-*Carboxymethyltropane*-3α,6β-*diol Betaine*.—(*a*) The lactone of (+)-N_b-carboxymethyl-3α,6β-dihydroxytropanium iodide (0·292 g.) was dissolved in water (20 ml.) and shaken with moist silver oxide (0·3 g.) for 6 hr.; the silver iodide was removed and washed with aqueous methanol. After removal of silver from the solution by hydrogen sulphide the solution was filtered and evaporated, and the residue crystallized from methanol (16 ml.), yielding the *betaine* as needles (0·17 g., 64%), m. p. 299—300° (decomp.), $[\alpha]_D^{20}$ −80° (*c* 0·3 in water) (Found: C, 55·4; H, 8·4; N, 6·3. $C_{10}H_{17}NO_4$ requires C, 55·8; H, 8·0; N, 6·5%).

(*b*) N_b-Ethoxycarbonylmethyl-3α,6β-dihydroxytropanium iodide (0·0725 g.) was dissolved in water (15 ml.) and shaken with moist silver oxide for 6 hr. After filtration, washing, precipitation with hydrogen sulphide, refiltration, and evaporation, the residue was recrystallized from methanol (4 ml.) to give the pure betaine (0·0476 g.; 82%), m. p. 298—300°, $[\alpha]_D^{20}$ −79·8° (*c* 0·2 in water) (Found: C, 55·3; H, 7·6; N, 6·5%).

Lactone of (+)-N_b-*Carboxymethyl*-3α,6β-*dihydroxytropanium Iodide from the Betaine*.—(−)-N_b-Carboxymethyltropane-3α,6β-diol betaine (0·3 g.) was dissolved in water (5 ml.) and the solution was evaporated with hydriodic acid to dryness under reduced pressure at 25°. The residue, when washed with dry acetone, afforded crystals (0·28 g.), m. p. 263—264° (decomp.), $[\alpha]_D^{20}$ +37·4° (*c* 2, in water). The substance gave no m. p. depression with lactone prepared directly from (−)-tropane-3α,6β-diol.

(±)-3α,6β-*Di-isovaleryloxytropane*.—(±)-Tropane-3α,6β-diol (0·8 g.) was refluxed with isovaleryl chloride (2·4 ml.) for 5 hr. The excess of chloride was removed *in vacuo* and the residue, in water (5 ml.), was extracted with ether (4 ml.). The aqueous solution was saturated with potassium carbonate and extracted with chloroform (10 × 3 ml.); the combined extracts were dried and evaporated to an oil (0·7 g.). The derived *picrate*, crystallized from dry ethanol, had m. p. 170° (Found: C, 52·3; H, 6·2; N, 9·8. $C_{24}H_{34}N_4O_{11}$ requires C, 52·0; H, 6·2; N, 10·1%).

(±)-*Valeroidine Hydrochloride*.—(±)-Di-isovaleryloxytropane (0·52 g.) was dissolved in a mixture of acetone (29 ml.) and 0·1N-sodium hydroxide (71 ml.). The solution was kept for 6 hr. at room temperature. It was neutralised with 0·1N-hydrochloric acid and evaporated at 50° after decolorisation with charcoal. The residue was dissolved in water (4 ml.) and the solution saturated with potassium carbonate and extracted with chloroform (10 × 5 ml.). The combined chloroform extracts were dried and evaporated. A viscous, pale-yellow oil (0·25 g.) was obtained. This oil (0·19 g.) gave with dry alcoholic hydrogen chloride, after recrystallization from alcohol–ether, a product of m. p. 180—182° undepressed by (±)-valeroidine hydrochloride [7] (Found: C, 56·2; H, 9·9; Cl, 12·6. Calc. for $C_{13}H_{24}ClNO_3$: C, 56·2; H, 8·7; Cl, 12·8%).

(±)-3α,6β-*Di-isovaleryloxytropane Hydrochloride*.—(−)-Tropane-3α,6β-diol (0·03 g.) was dissolved in freshly distilled isovaleryl chloride (0·1 ml.), and the solution kept at 150° for 2 hr. Excess of chloride was evaporated and the remaining oily crystals recrystallized from alcohol–ether, to give white needles (0·0378 g.), m. p. 124—125°, $[\alpha]_D^{20}$ +2·66° (*c* 3·78 in anhydrous ethanol) (Found: C, 59·9; H, 8·7. $C_8H_{32}ClNO_4$ requires C, 59·7; H, 8·9%). The hydrobromide was prepared by Stoll, Lindenmann, and Jucker.[8]

(−)-*Valeroidine*.—(+)-3α,6β-Di-isovaleryloxytropane hydrochloride (0·03 g.) was dissolved in a mixture of acetone (1·5 ml.) and 0·1N-sodium hydroxide (3·5 ml.) and was kept at room temperature for 5 hr. The solution was neutralized with 0·1N-hydrochloric acid and evaporated at 30° *in vacuo* to about 1 ml. The solution was saturated with potassium carbonate and shaken with chloroform (6 × 1 ml.). Evaporation of the dried ($MgSO_4$) extract afforded valeroidine (0·01 g.), m. p. 80° undepressed by natural valeroidine.[12] The hydrobromide, prepared with azeotropic hydrobromic acid and recrystallized from ethanol–ether (0·0008 g.), had m. p. 170—171° alone or on admixture with the hydrobromide of authentic natural valeroidine (Found: C, 48·05; H, 7·2. Calc. for $C_{13}H_{24}BrNO_3$: C, 48·45; H, 7·5%).

(G. F.) Stereochemical Laboratory, The Academy of Sciences, Budapest, Hungary.
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[*Received, March 13th*, 1961.]

[12] Barger, Martin, and Mitchell, *J.*, 1937, 1820.

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632. *The Stereochemistry of the Tropane Alkaloids. Part XIV.*[1] *The Absolute Configuration of (−)-Tropic Acid, Hyoscyamine, and Hyoscine.*[2]

By Gábor Fodor and György Csepreghy.

The absolute configuration of (−)-tropic acid has been established by its correlation with (−)-alanine. According to the Cahn–Ingold–Prelog convention, natural tropic acid possesses the (*S*)-configuration.

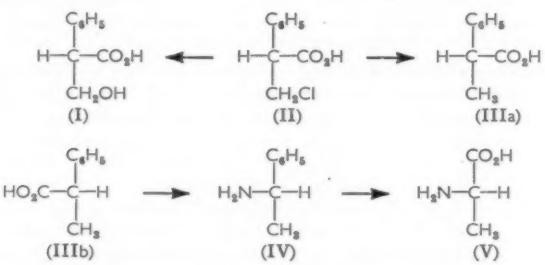
(−)-Tropic acid is the acidic building stone of a number of important alkaloids, amongst others hyoscyamine and hyoscine. In order to obtain a deeper insight into the biosynthesis and mode of physiological action of the latter compounds, the establishment of the absolute configuration of (−)-tropic acid was necessary.

The only approach to the configuration of tropic acid reported hitherto is that by Freudenberg *et al.*,[3] based on the dextro-shift of optical rotational values observed when the acid is converted into the ester, parallel to that experienced by passing from (−)-mandelic acid and (−)-atrolactic acid to the corresponding esters. The tentative projection formula (I) for (−)-tropic acid was advanced by Freudenberg *et al.* with serious reservations: " ob derartige Schlüsse gezogen werden dürfen, und ob diese Betrachtung verallgemeinert werden darf, muss an weiterem Material geprüft werden." [3]

To check the correctness of this, the correlation of (−)-tropic acid with either (+)- or (−)-alanine was attempted.

β-Chlorohydratropic (α-chloromethyl-α-phenylacetic) acid (II) was resolved by McKenzie and Strathern [4] more than three decades ago, and the lævorotatory acid was subsequently hydrolysed to (−)-tropic acid (I), the reaction being accompanied by slight racemization; hydrolysis with aqueous ammonia gave (−)-tropamide in a higher state of optical purity.

On the other hand, (+)-α-phenylpropionic acid (IIIb) was subjected to the Curtius reaction, to give (−)-1-phenylethylamine [5] (IV), and the *N*-benzoyl derivative was oxidized, in turn,[6] to (+)-alanine (V).



Since the Curtius method involves a 1,2-carbanion shift, and proceeds, with the exception of a single case,[8] with retention of configuration [7,11] within the migrating group, the correlation of (+)-α-phenylpropionic acid (IIIb) with natural (+)-alanine can be regarded as decisive.

[1] Part XIII, preceding paper.
[2] Preliminary communication, *Tetrahedron Letters*, 1959, No. 7, 16.
[3] Freudenberg, Todd, and Seidler, *Annalen*, 1933, **501**, 206.
[4] McKenzie and Strathern, *J.*, 1925, **127**, 86.
[5] Bernstein and Whitmore, *J. Amer. Chem. Soc.*, 1939, **61**, 1324.
[6] Leithe, *Ber.*, 1931, **64**, 2827.
[7] Alexander, " Principles of Ionic Organic Reactions," Chapman and Hall, London, 1950, p. 118.
[8] Skita and Rössler, *Ber.*, 1939, **72**, 461.

Vol. 1961, page 3223, line 3 from end of text. *Insert* /1—2 mm. *after* The distillate (0·2 g., 56·2%) had b. p. 115°.

In consequence, according to the convention of Cahn *et al.*,[9] (+)-α-phenylpropionic acid is designated as (*S*) (IIIb), whilst the (*R*)-configuration corresponds to the lævorotatory form (IIIa).

The single missing link between tropic acid and alanine was now the correlation of (—)-β-chlorohydratropic acid (II) with either (*S*)- or (*R*)-α-phenylpropionic acid. This work has been completed recently in the authors' laboratory.

β-Chlorohydratropic acid, obtained from atropic acid,[10] was resolved, with codeine in place of the morphine used by McKenzie *et al.*[4] The lævorotatory acid, m. p. 62°, gave correct rotational values. Hydrogenolysis of this compound over palladized charcoal in ethyl acetate, in the presence of barium hydroxide, resulted in the formation (*R*)-(—)-α-phenylpropionic acid. The Cahn–Ingold–Prelog convention [9] then gives the configuration (*S*)-(—)-tropic acid (I) for the lævorotatory form.

Experimental

(±)-β-*Chlorohydratropic* (α-*Chloromethyl-α-phenylacetic*) *Acid* (II).—This was prepared essentially by the method of McKenzie and Wood [10] by passing dry hydrogen chloride into atropic acid (6·1 g., 0·041 mol.) in dry ether (122 ml.) for 6 hr. at 25°. The ethereal solution was washed with water and dried ($CaCl_2$), and the solvent removed, to give crystals (6·9 g., 90·8%), m. p. 86—88°.

Resolution. Codeine (6·34 g., 0·0212 mol.) and (±)-β-chlorohydratropic acid (2·7 g., 0·0147 mol.) were dissolved separately in methanol (30 ml. each), the solutions were mixed at 65°, and the mixture was kept for 2 days at 60°. Filtration then afforded crystals (4 g.) of codeine (—)-β-chlorohydratropate, which, after being boiled with methanol (50 ml.), gave a pure product, m. p. 138° (decomp.), $[\alpha]_D^{20}$ −95° (*c* 0·4 in methanol) (Found: C, 67·9; H, 6·3; N, 2·7. $C_{27}H_{30}ClNO_5$ requires C, 67·0; H, 6·2; N, 2·9%).

This salt was treated with 10% hydrochloric acid (70 ml.) and then extracted several times with ether (total 250 ml.). The combined ethereal extracts were washed with water, dried ($CaCl_2$), and evaporated. The residual crystals (0·8 g., 59·2%) had m. p. 62°, $[\alpha]_D^{20}$ −115° (*c* 0·3 in ethanol). McKenzie and Wood [10] reported m. p. 62°, $[\alpha]_D^{20}$ −115° (*c* 0·4 in methanol).

Hydrogenolysis of (—)-β-*Chlorohydratropic Acid to* (—)-α-*Phenylpropionic Acid.*—Barium hydroxide dihydrate (2 g., 0·00965 mol.) and 10% palladized charcoal (0·5 g.) were shaken in ethyl acetate (60 ml.) in a hydrogen atmosphere. After the uptake of hydrogen by the catalyst had ceased, (—)-β-chlorohydratropic acid (0·44 g., 0·002375 mol.) in ethyl acetate (40 ml.) was added and the mixture hydrogenated at 26°/1 atm. When absorption (60 ml.; calc., 55·5 ml.) was complete, the solution was acidified with 5N-hydrochloric acid to pH 1 and filtered. The filtrate was evaporated to dryness and the residual oil distilled *in vacuo*. The distillate (0·2 g., 56·2%) had b. p. 115°, $[\alpha]_D^{20}$ −76° (*c* 0·79 in 96% ethanol) (Found: C, 72·2; H, 6·7. Calc. for $C_9H_{10}O_2$: C, 72·0; H, 6·7%).

We are indebted to Dr. Eva Fodor-Varga for the microanalyses.

Stereochemical Research Laboratory, The Hungarian Academy of Science, Budapest, Hungary. [*Received, March 13th*, 1961.]

[9] Cahn, Ingold, and Prelog, *Experientia*, 1956, **12**, 81.
[10] McKenzie and Wood, *J.*, 1919, **115**, 828.
[11] Arcus and Kenyon, *J.*, 1938, 485.

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633. *Reactions of Sulphoxides with Some Group III and IV Halides.*

By M. F. Lappert and J. K. Smith.

The reactions of certain sulphoxides (R_2 in R_2SO = Me_2, Pr^iBu^t, Bu^t_2, or Ph_2) with boron, silicon, or tin halides have been investigated. As a rule, molecular addition compounds were obtained, but anomalous behaviour was noted in certain cases (Me_2SO–BCl_3, Me_2SO–$SiCl_4$, and Ph_2SO–$SiCl_4$) to give chloro-substituted sulphides or their derivatives (including $Cl{\cdot}CH_2{\cdot}S{\cdot}CH_2{\cdot}BOCl$). A self-consistent picture of sulphoxide–halide reactions is presented. The infrared spectra of the sulphoxides and their complexes have been investigated and detailed assignments are presented for the aromatic derivatives; structural and stereochemical implications are discussed and structure (II) is confirmed.

Dimethyl sulphoxide has been used extensively as a solvent, because it has been recognised as highly polar. Until recently, the properties of sulphoxides as ligands had not, however, been explored [apart from some early references to adducts of diaryl sulphoxides with cadmium iodide, chloroplatinic, chloroauric, and cyanoferrous acid,[1] and with iron(III) chloride [2]]. Several papers have appeared, within the last few months, on co-ordination compounds of dimethyl sulphoxide with transition-metal derivatives,[3,4] as well as with halides of certain representative elements [zinc chloride and bromide (also nitrate and perchlorate), cadmium chloride,[3] boron fluoride,[3a,5] aluminium chloride,[3a] silicon,[6a] germanium(IV), and tin(IV) fluorides, tin(IV) chloride,[3] and antimony-(III) and -(IV) chlorides [7]]; a 1 : 1 adduct of diphenyl sulphoxide and antimony(V) fluoride has also been prepared.[4] Dimethyl sulphoxide was said to form complexes with silicon tetrachloride and with trichlorosilane.[6b] This prompts us to present our results on the reactions of boron, silicon, and tin(IV) halides with dimethyl, isopropyl t-butyl, di-t-butyl, and diphenyl sulphoxides and on the infrared spectra of these sulphoxides and of certain of their complexes.

Dimethyl sulphoxide is clearly a powerful donor (although weaker in this respect than triphenylphosphine oxide or diphenyl selenoxide [7]) because of the wide range of compounds with which it forms molecular complexes. That it, unlike the sulphide or sulphone, formed a stable complex with boron trifluoride, led Laughlin [5] to suggest that the oxygen and not the sulphur was the donor atom. This was also the conclusion of Cotton and co-workers [3] with respect to some thirty-four complexes, and only for palladium(II) chloride was sulphur-donation considered probable. Their evidence was based on visible and infrared spectra, magnetic measurements, and arguments based on steric strain.

Interaction of a sulphoxide and a halide in an inert solvent, at low temperature, led to instant precipitation of the appropriate complex [1 : 1 in stoicheiometry for boron halides (F,Cl) and 2 : 1 for tin(IV) halides (Cl,Br,I)]. There were three exceptions to this behaviour [see (1)—(3)].

$$2Me_2SO + SiCl_4 \longrightarrow 2MeS{\cdot}CH_2Cl + SiO_2 + 2HCl \quad \ldots\ldots (1)$$

$$\left.\begin{array}{l} Me_2SO + BCl_3 \longrightarrow MeS{\cdot}CH_2Cl + \tfrac{1}{3}(BOCl)_3 + HCl \\ MeS{\cdot}CH_2Cl + \tfrac{1}{3}(BOCl)_3 \longrightarrow MeS{\cdot}CH_2Cl,BOCl \\ MeS{\cdot}CH_2Cl + BCl_3 \longrightarrow MeS{\cdot}CH_2Cl,BCl_3 \end{array}\right\} \quad \ldots\ldots (2)$$

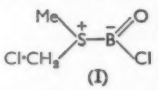
$$2Ph_2SO + SiCl_4 \longrightarrow 2p\text{-}Cl{\cdot}C_6H_4{\cdot}SPh + SiO_2 + 2HCl \quad \ldots\ldots (3)$$

[1] Pickard and Kenyon, *J.*, 1907, **91**, 896.
[2] Hofman and Ott, *Ber.*, 1907, **40**, 4930.
[3] (*a*) Cotton and Francis, *J. Amer. Chem. Soc.*, 1960, **82**, 2986; (*b*) Cotton, Francis, and Horrocks, *J. Phys. Chem.*, 1960, **64**, 1534; (*c*) Horrocks and Cotton, *Spectrochim. Acta*, 1961, **17**, 134.
[4] (*a*) Muetterties, *J. Amer. Chem. Soc.*, 1960, **82**, 1082; (*b*) Schläfer and Schaffernicht, *Angew. Chem.*, 1960, **72**, 618.
[5] Laughlin, *J. Org. Chem.*, 1960, **25**, 864.
[6] (*a*) Gutmann and Utvary, *Monatsh.*, 1959, **90**, 706; (*b*) Gutmann, quoted in ref. 4*b*.
[7] Lindqvist and Zackrisson, *Acta Chem. Scand.*, 1960, **14**, 453.

The boron trichloride–dimethyl sulphoxide system has previously been examined by Cotton and Francis,[2a] and complex formation (Me_2SO,BCl_3, or more probably $Me_2SO,2BCl_3$) was then tentatively proposed. Our interpretation (reactions 2) rests on (i) analogy with reaction (1) and with thionyl chloride–sulphoxide reactions, and (ii) identification of the chloromethyl methyl sulphide complexes of boron oxychloride and trichloride. As to (i), Bordwell and Pitt [8] showed that thionyl chloride reacts with alkyl (or aryl) methyl sulphoxides to form hydrogen chloride, sulphur dioxide, and alkyl (or aryl) chloromethyl sulphides. As to (ii), the main non-volatile product of the boron trichloride–dimethyl sulphoxide reaction was the oxychloride complex (insoluble in methylene chloride), and a subsidiary one was the trichloride complex. The latter was also synthesised from the sulphide and boron trichloride. From either complex, the sulphide could be displaced by reaction with quinoline, confirming the structural assignments.

Sulphide complexes of boron trichloride are not new,[9] but the introduction of an α-chlorine atom might have been expected so seriously to weaken the donor strength of the sulphide as to prevent isolation of a complex (as it does in corresponding ethers [10]). In fact, the saturation vapour pressure of chloromethyl methyl sulphide–boron trichloride is 10 mm. at 20°.

The isolation of a boron oxychloride complex is interesting, since the free oxychloride is so unstable as to have had its existence questioned,[11] although spectroscopic evidence for its existence as a boroxole, $(ClBO)_3$, has now been obtained.[12] The only prior report of a boron oxychloride stabilised by co-ordination has been of the pyridine adduct.[13] The oxychloride–sulphide complex is thought to be more stable than the trichloride–sulphide complex, because (i) it is the major product of reactions (2), suggesting that, in the competition for sulphide, the oxychloride is the stronger acceptor, and (ii) the saturation vapour pressure of the oxychloride complex is negligible at room temperature. These observations are consistent with a monomeric structure (I) for the oxychloride complex, providing, so far as we are aware, a unique example of a co-ordination compound having a multiply bonded boron atom. Evidence for structure (I) also comes from the infrared spectrum, which shows strong (but broad) absorption at 1400—1450 cm.$^{-1}$, almost certainly due to the B–O stretching vibration. The B–O stretching frequency in three-co-ordinate boron esters, >B–OR, falls at ~1350 cm.$^{-1}$, and in these compounds the B–O bonds already have appreciable double-bond character due to p_π–p_π-bonding.[14,15]



(I)

Reaction (3) has close analogy to early observations by Michaelis and his co-workers [16] on the behaviour of diphenyl sulphoxide with thionyl or phosphorus(v) chloride. Reaction (3) has been independently discovered by Issleib and Tzschach,[17] and is included in the present paper because of its relevance to the mechanism (4) proposed for sulphoxide–halide reactions, and because of the characterisation of the products.

It appears that, in general, the reaction of a sulphoxide and an electron-deficient metal or non-metal halide, MX-, proceeds by a nucleophilic attack of the former at M to produce a complex; unless the M–X bond is highly polarisable, in which case M–X heterolysis takes place (either synchronously or separately) and the next step is probably a 1 : 3 shift of halogen by an S_Ni mechanism (see reaction 4). The subsequent fate of the chlorosulphonium chloride is determined by the nature of the group R, (alkyl or aryl).

That sulphoxides are strong donors was also shown by the formation of a stable complex

[8] Bordwell and Pitt, *J. Amer. Chem. Soc.*, 1955, **77**, 572.
[9] Phillips, Hunter, and Sutton, *J.*, 1945, 146; Lappert, *J.*, 1953, 2784.
[10] Edwards, Gerrard, and Lappert, *J.*, 1957, 377.
[11] Martin, *Chem. Rev.*, 1944, **44**, 461.
[12] Goubeau and Keller, *Z. anorg. Chem.*, 1953, **272**, 203.
[13] Lappert, *J.*, 1953, 667.
[14] Werner and O'Brien, *Austral. J. Chem.*, 1955, **8**, 355.
[15] Bellamy, Gerrard, Lappert, and Williams, *J.*, 1958, 2412.
[16] Michaelis and Godchoux, *Ber.*, 1891, **24**, 757; Loth and Michaelis, *Ber.*, 1894, **27**, 2540.
[17] Issleib and Tzschach, *Z. anorg. Chem.*, 1960, **305**, 198.

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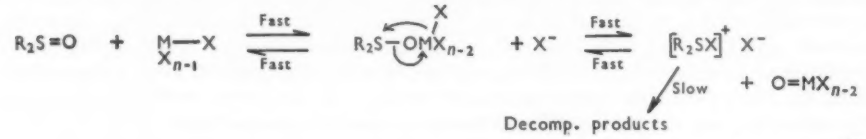
with tin(IV) iodide, which is normally a poor acceptor. On the other hand, dimethyl sulphoxide is evidently not as strong a base as pyridine, with respect to tin(IV) chloride as reference Lewis acid: it could not compete effectively with pyridine, when the chloride



. . . . . (4)

was added to a mixture of the two bases in methylene chloride [in which both the pyridine– and dimethyl sulphoxide–tin(IV) chloride complexes are insoluble].

Infrared Spectra of the Sulphoxides and their Complexes, and the Structure of the Complexes.—The infrared spectra of a number of sulphoxides have been examined by Barnard, Fabian, and Koch,[18] and they established that the strong absorption band at ~1050 cm.$^{-1}$ arose from the S–O stretching vibration. The C–S stretching vibration in diphenyl sulphoxide was tentatively assigned[19] to a band at 684 cm.$^{-1}$. No attempt at a full co-ordinate treatment, with assignment of fundamentals, has yet been published even for the lowest homologue, dimethyl sulphoxide (although this is now in hand[3b,3c]), and we therefore can do little else than describe the spectra of the sulphoxides and the changes that occur on complex-formation, in particular noting shifts in the S–O stretching frequency (Table 1). These results may be regarded as supplementary to recent reports by Cotton, Francis, and Horrocks[3b] on dimethyl sulphoxide complexes with cadmium, zinc, and tin(IV) chloride, cadmium bromide, and certain transition-metal derivatives.

TABLE 1. S–O *Stretching frequencies in sulphoxides and their complexes.*[a,b]

Compound	νS–O (cm.$^{-1}$) (mull[c])	νS–O (cm.$^{-1}$) (KBr disc)	$-\Delta\nu$[d] (cm.$^{-1}$)	Compound	νS–O (cm.$^{-1}$) (mull[c])	νS–O (cm.$^{-1}$) (KBr disc)	$-\Delta\nu$[d] (cm.$^{-1}$)
Me_2SO,BF_3	938	—	129	Pr^iBu^tSO,BCl_3	913	—	133
$(Me_2SO)_2,SnCl_4$	920, 905	919, 905	147, 162	Bu^t_2SO,BCl_3 ...	919	—	114
$(Me_2SO)_2,SnBr_4$	911, 903	913, 903	155, 164	Ph_2SO,BCl_3 ...	887	—	159
$(Me_2SO)_2,SnI_4$...	924, 904	920, 902	145, 164	$(Ph_2SO)_2,SnCl_4$	937, 913	937, 913	109, 133

[a] νS–O in (i) Me_2SO (2% solution in CCl_4) at 1067 cm.$^{-1}$, (ii) Pr^iBu^tSO (5% solution in CCl_4) at 1046 cm.$^{-1}$, (iii) Bu^t_2SO (6% solution in CCl_4) at 1033 cm.$^{-1}$, and (iv) Ph_2SO (5% solution in CCl_4) at 1046 cm.$^{-1}$. [b] The results are accurate to ±5 cm.$^{-1}$. [c] In liquid paraffin. [d] Average values.

With diphenyl sulphoxide, it is possible to go further because, with the very detailed discussion available of the various aromatic absorptions of the monohalogenobenzenes,[20] we can assign (Table 2) all the bands in the spectrum of diphenyl sulphoxide and of its complexes, with reasonable certainty. An interesting feature of these spectra is the splitting of the out-of-phase CH-aromatic deformation (B_2) into a doublet, with the two bands separated by about 20 cm.$^{-1}$. A similar observation[21] was made for spectra of compounds having two phenyl groups attached to a three-co-ordinate boron atom, $Ph_2B{\cdot}\dot{\ddot{Y}}$ (Y = Hal, OR, OH, etc.), and for *NN*-diphenylacetamide and its boron trichloride complex.[22] On the other hand, such splitting is not invariably present in compounds having two phenyl groups joined to a common atom, *e.g.*, not in diphenylamine. It appears possible that the splitting arises from a coupling of modes caused by the close approach of the *ortho*-hydrogen atoms and this might be significant only when the common atom is multiply bonded to an adjacent one (as, *e.g.*, in $Ph_2\bar{B}{=}\dot{\ddot{Y}}$, Ph_2SO, etc.).

[18] Barnard, Fabian, and Koch, *J.*, 1949, 2442.
[19] Cymerman and Willis, *J.*, 1951, 1332.
[20] Whiffen, *J.*, 1956, 1350.
[21] Abel, Gerrard, and Lappert, *J.*, 1957, 3833.
[22] Gerrard, Lappert, Pyszora, and Wallis, *J.*, 1960, 2144.

TABLE 2. *Diphenyl sulphoxide and its tin*(IV) *chloride complex; absorption bands* (*cm.*$^{-1}$) *and assignments.*

Ph_2SO [a]	$(Ph_2SO)_2,SnCl_4$ [b]	Assignment	Ph_2SO [a]	$(Ph_2SO)_2,SnCl_4$ [b]	Assignment
3053 (1) [c]	3053 (1) [d]	C–H stretch (A_1)	1155 (12)	1157 (13)	C–H deformn. (B_1)
1949 (2)	1980 (2)	Aromatic overtone and combination bands	1089 (13)	1078 (14)	Mass-dependent (A_1)
1876 (3)	1887 (3)		1071 (14)	1073 (15)	C–H deformn. (B_1)
1797 (4)	1818 (4)		1046 (15)	937 (18)	S–O stretch
1742 (5)	1795 (5)			913 (19)	
1580 (6)	1580 (6)	C–C stretch (A_1) (masking B_1)	1020 (16)	1018 (16)	C–H deformn. (A_1)
			996 (17)	995 (17)	Ring deformn. (A_1)
1475 (7)	1473 (7)	C–C stretch (A_1)	911 (18)	913 (19)	C–H deformn. (B_1) masked by νS–O
1443 (8)	1443 (8)	C–C stretch (B_1)			
1321 (9)	1326 (9)	C–C stretch (B_1)	755 (19) [b]	763 (20)	C–H deformn. (B_2)
1302 (10)	1307 (10)	C–H deformn. (B_1)	735 (20) [b]	745 (21)	
	1290 (11)		692 (21) [b]	694 (22)	Ring deformn. (B_2)
1164 (11)	1173 (12)	C–H deformn. (A_1)	684 (22) [b]	679 (23)	C–S stretch

[a] Solution (5%) in CCl_4. [b] KBr disc (A in Fig. 1). [c] Numbers in parentheses refer to location in Fig. 1. [d] Numbers in parentheses refer to location in Fig. 2.

The spectra of diphenyl sulphoxide (Fig. 1) and its tin(IV) chloride complex (Fig. 2) are reproduced and the location of absorption bands is indicated in Table 2, whilst the spectra of dimethyl, isopropyl-t-butyl, and di-t-butyl sulphoxide and some of their complexes

Infrared spectra of (FIG. 1) *diphenyl sulphoxide in carbon tetrachloride and* (A) *Nujol mull, and* (FIG. 2) *bis(diphenyl sulphoxide)tin*(IV) *chloride in a* KBr *disc.*

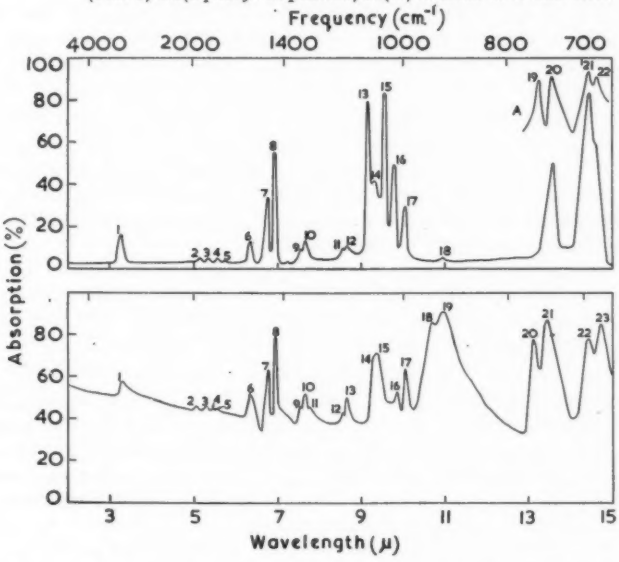


FIG. 1.

FIG. 2.

are described in Table 5. It is clear that, on complex-formation; the only significant change in the diphenyl sulphoxide series is the large shift of the S–O stretching vibration to lower frequency. This is also evident with the aliphatic sulphoxides and their complexes, although further shifts are apparent in the 900—1150 cm.$^{-1}$ region. With the boron trichloride complexes, absorption bands due to B–Cl stretching vibration are readily distinguished (Table 3) [cf. $CH_3{\cdot}CO{\cdot}NMe_2,BCl_3$ (ref. 22) at 777, 753, and 713 cm.$^{-1}$; and RCN,BCl_3 (ref. 23) at 778, 733, and 711 cm.$^{-1}$], whilst the Sn–Hal stretching frequencies would not be expected to fall within the rock-salt region.

[22] Gerrard, Lappert, Pyszora, and Wallis, *J.*, 1960, 2182.

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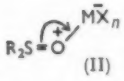
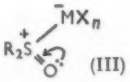
TABLE 3. B–Hal *Stretching frequencies in* R_2SO,BCl_3.

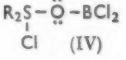
Compound	$Pr^iBu^tSO\cdot BCl_3$	Bu^t_2SO,BCl_3	Ph_2SO,BCl_3
νB–Cl	760, 714	767, 736	775, 723, 709

In the low-frequency region, absorption, probably due to the C–S stretching vibration, is also apparent in the aliphatic compounds [Me_2SO 686; Me_2SO,BF_3 685; $(Me_2SO)_2,SnCl_4$ 724; $(Me_2SO)_2,SnBr_4$ 724; $(Me_2SO)_2,SnI_4$ 719; Bu^t_2SO 682; Bu^t_2SO,BCl_3 671; and Pr^iBu^tSO,BCl_3 681 cm.$^{-1}$].

Possible structures for the sulphoxide complexes are (II) and (III); structure (IV) is


(II)


(III)


(IV)

only feasible for the boron trichloride adducts, because the B–Cl bond, unlike the other M–Hal bonds, is highly polarisable. It is relevant to consider structure (IV), because examples of boron trichloride addition to multiply bonded compounds are known (*e.g.*, for ketones [24] and certain olefins [25]).

The S–O bond in a sulphoxide may be regarded as substantially a double bond, with p_π–d_π ($\bar{S} \leftarrow \overset{+}{O}$) bonding from oxygen to sulphur superimposed on the SO σ-bond ($\overset{+}{S}$–$\bar{O}$) (for bibliography, see ref.[3a]). Structure (II) for the complex implies a lengthening of the S–O bond (decrease in p_π–d_π bonding) in the complex compared with the free ligand and hence a decrease in the S–O stretching frequency would be expected; conversely, structure (III) requires an increase in S–O stretching frequency. This argument ignores (i) the mass effect of the acceptor, and (ii) the possibility of coupling between the SO and the MO oscillator. However, both these would cause an increase in the S–O stretching frequency and the experimentally observed substantial decreases (Table 2), therefore, unequivocally demonstrate that the oxygen is the donor atom in these sulphoxide co-ordination compounds. Structure (IV) may be discounted because the S–O single bond stretching vibration would then fall at much lower frequency than ~900 cm.$^{-1}$ and the B–Cl stretching vibration at much higher frequency [15,21] than ~700 cm.$^{-1}$.

It is noteworthy that the SO absorption is only split into a doublet in the spectra of those compounds in which there is a 2 : 1 ligand : acceptor ratio [this had not previously been noticed [3b] in the spectrum of $(Me_2SO)_2,SnCl_4$], and this might be taken as an indication that the ligands are placed *cis* to one another in the octahedral complexes. Thus, coupling between the two S–O vibrations through the metal (Sn) atom would give rise to symmetric and antisymmetric modes, and, whereas in a *trans*-complex the former mode would be infrared-degenerate, in a *cis*-complex they would both be infrared-active. However, as the spectral measurements were made on solid specimens (the complexes were insoluble in all the common non-polar organic solvents), other explanations are possible—particularly the non-equivalence of ligands in the crystal, whether in a *cis*- or a *trans*-complex.

EXPERIMENTAL

General Procedures.—The sulphoxides were purified by removal of water as the benzene azeotrope, followed by distillation, or by recrystallisation as appropriate. The halides were redistilled and recondensed (BCl_3) or recrystallised (SnI_4). Solvents were dried (P_2O_5) and redistilled. Halogen, boron, and tin (as appropriate) in complexes were estimated in an enclosed system, acidimetrically as hydrogen halide (Methyl Red) and boric acid (phenolphthalein in presence of mannitol) after hydrolysis with cold water; or as hydrogen halide (Volhard); or, for tin, by reduction with iron wire and hydrochloric acid and subsequent

[24] Gerrard and Lappert, *Chem. Rev.*, 1958, **58**, 1081.
[25] Joy and Lappert, *Proc. Chem. Soc.*, 1960, 353.

iodometric determination in a nitrogen atmosphere. Pyridine was estimated by steam-distillation from potassium hydroxide and titration of the distillate with sulphuric acid (Bromophenol Blue). Microanalyses (C, H, and S) were carried out by Mr. V. Manohin and his staff, and we offer them our best thanks.

Infrared spectra were recorded with a Perkin–Elmer 21 spectrophotometer, with sodium chloride optics. Samples were studied as discs (KBr), mulls (liquid paraffin and hexachlorobutadiene), and solutions (CCl_4), as appropriate.

Precautions were taken during manipulative operations to avoid contamination by atmospheric moisture. M. p.s were taken in sealed capillary tubes.

Preparation of the Complexes.—These were obtained by dropwise addition of the sulphoxide in methylene chloride to the cooled (0°) halide (in appropriate stoicheiometry) in the same

TABLE 4.

			Found (%)				Required (%)			
Complex	Yield (%)	M. p.*	C	H	Hal	M	C	H	Hal	M
$(Me_2SO)_2,SnCl_4$	97	270—300°	12·0	3·1	34·0	28·6	11·5	2·9	34·0	28·5
$(Me_2SO)_2,SnBr_4$	98	198—204	8·2	1·9	53·6	20·1	8·1	2·1	53·8	20·0
$(Me_2SO)_2,SnI_4$	100	167—168	6·3	1·4	65·2	15·4	6·1	1·5	64·9	15·2
Pr^iBu^tSO,BCl_3	75	†	33·3	6·4	37·4	3·8	31·7	6·1	40·0	4·1
Bu^t_2SO,BCl_3	92	†	32·9	6·2	36·0	3·7	34·4	6·5	38·1	3·9
Ph_2SO,BCl_3.....	100	†	47·1	3·9	32·5	3·4	45·1	3·2	33·3	3·4
$(Ph_2SO)_2,SnCl_4$	100	224—226	44·8	3·3	21·0	17·5	43·4	3·0	21·3	17·8

* These may be decomposition temperatures. † These did not become transparent, even at 300°.

solvent; reactions were carried out on 0·01—0·1-molar scale and the total volume of solvent was 2—4 times the combined weights of reactants. Evolution of heat accompanied the formation of the white [or violet, in the case of the tin(IV) iodide] *complex*, which was filtered off, washed with methylene chloride, and freed from solvent at 20°/10 mm. The results are summarised in Table 4. Dimethyl sulphoxide–boron trifluoride [5] was characterised merely by its infrared spectrum and by its formation in quantitative yield.

Interaction of Silicon Tetrachloride and Diphenyl Sulphoxide.—Silicon tetrachloride (2·78 g., 1 mol.) in methylene chloride (10 ml.) was added to the sulphoxide (6·60 g., 2 mol.) in the same solvent (40 ml.) at 0°. There was a vigorous reaction. Hydrogen chloride was evolved and the white solid deposit of silica (0·98 g., 100%) ($\nu_{max.}$ 1149 and 1081 cm.$^{-1}$) was filtered off. Removal of solvent from the filtrate at 20°/10 mm. gave *p*-chlorophenyl phenyl sulphide (7·10 g., 99%). On distillation, this afforded the pure sulphide (4·30 g.), b. p. 154°/7 mm., n_D^{20} 1·6353. The infrared spectrum of this sulphide was very similar to that of diphenyl sulphide, except for a strong band at 817 cm.$^{-1}$ (C–Cl) and bands at 1946 and 1883 cm.$^{-1}$ (characteristic of a *para*-substituted phenyl group).

Interaction of Silicon Tetrachloride and Dimethyl Sulphoxide.—Dimethyl sulphoxide (15·4 g., 1 mol.) was added dropwise to silicon tetrachloride (33·5 g., 1 mol.) at 0°. Evolution of hydrogen chloride accompanied the exothermic reaction. Distillation of the mixture afforded chloromethyl methyl sulphide (14·6 g., 77%), b. p. 106—107°, n_D^{20} 1·4957 ($\nu_{max.}$ 1149 and 1081 cm.$^{-1}$), and a residue of silica (12·0 g., 100%).

Interaction of Boron Trichloride and Dimethyl Sulphoxide.—Dimethyl sulphoxide (3·1 g., 1 mol.) in methylene dichloride (10 ml.) was added dropwise (30 min.) to boron trichloride (4·65 g., 1 mol.) in the same solvent (10 ml.) at 0°. The reaction was highly exothermic. Hydrogen chloride was evolved (and was identified spectroscopically) and a white crystalline deposit of the complex, *boron oxychloride–chloromethyl methyl sulphide* (6·1 g., 97%) (Found: C, 16·5; H, 3·5; Cl, 43·6; S, 19·15; B, 6·5. $C_2H_5Cl_2OSB$ requires C, 15·12; H, 3·17; Cl, 44·65; S, 20·18; B, 6·8%), was formed, which was filtered off, washed with methylene dichloride (3 × 5 ml.), and freed from solvent at 20°/10 mm.

In other experiments, the yield of complex was less (~85%), and the filtrate, after removal of solvent, afforded the sulphide–trichloride complex, identified analytically and by comparing its infrared spectrum with that of the authentic sample.

In a further experiment, dimethyl sulphoxide (13·0 g., 1 mol.) in methylene dichloride (10 ml.) was added to boron trichloride (14·5 g., 1 mol.) in the same solvent (10 ml.) at 0°. The

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complex was not isolated, but to the reaction mixture at 0° quinoline (5 ml.) in methylene dichloride was added. Heat of reaction accompanied the liberation of chloromethyl methyl sulphide from its boron oxychloride complex. Fractional distillation gave the pure sulphide (2·6 g., 70%), b. p. 106—107°, n_D^{20} 1·4957.

Interaction of Boron Trichloride and Chloromethyl Methyl Sulphide.—Boron trichloride (4·1 g., 1·6 mol.) was added to chloromethyl methyl sulphide (2·1 g., 1 mol.) at −78°. The

TABLE 5. *Principal absorption bands (max. in cm.$^{-1}$) in sulphoxides and complexes.*

Me_2SO [a]	$(Me_2SO)_2,SnCl_4$ [b]	Pr^iBu^tSO [c]	Pr^iBu^tSO,BCl_3 [d]	$Bu^t{}_2SO$ [e]	$Bu^t{}_2SO,BCl_3$
2994m	3003w	2963s	2924s [h]	2959vs	2972s [h]
2915m	2914w	2941m(sh)	2857s [h]	2915s(sh)	1477m(sh) [h]
1618w	1422m	2865m	1488m(sh) [h]	1466s	1464s [h]
1433vs	1408m	1471m(sh)	1473m(sh) [h]	1447s(sh)	1397m [h]
1412s	1395m	1458m	1460s [h]	1385m	1374s [h]
1401s	1323w	1383m(sh)	1443s(sh) [h]	1364vs	1220vw
1312s	1302w	1365m	1403m [h]	1279m	1190vw
1302s	1033m	1294w	1385m [h]	1223m	1155w
1145w	987m	1232w	1376m [h]	1217m	1078vw
1067vvs	947m(sh)	1175w	1372m(sh)	1166s	1029vw
1008s	919s	1155w	1235w	1099m	919s
942s	905s	1115w	1167m	1072m(sh)	820vw
917s	724w	1046s	1153m	1033vvs	800w
883m		1031m(sh)	1109vw	1018vs	767vw
686s		954vw	1052m	941w	736m
		935vw	1024w	931w	671m
		871vw	913vs	787w [g]	
		864vw	830w	682w	
		789vw [g]	810m		
			802m		
			763s(sh)		
			760s		
			714m		
			681s		

[a] 2% in CCl_4. [b] KBr disc. [c] 5% in CCl_4 and liquid paraffin mull (*g*). [d] Mulls in hexachlorobutadiene (*h*) and liquid paraffin. [e] 6% in CCl_4 and liquid paraffin mull (*g*). [f] Mulls in hexachlorobutadiene (*h*) and liquid paraffin.

white crystalline complex, *boron trichloride–chloromethyl methyl sulphide* (4·5 g., 98%) (Found: Cl, 65·6; B, 5·0. $C_2H_5Cl_4SB$ requires Cl, 66·3; B, 5·06%), was isolated by removal of the excess of boron trichloride at −78°/5 mm. At room temperature and under a vacuum, the complex lost boron trichloride rapidly to give a yellow gum.

Addition to the complex (4·5 g.) of quinoline (5 ml.) at 0°, and distillation afforded chloromethyl methyl sulphide (2·54 g., 62%), b. p. 106—107°, n_D^{20} 1·4957.

Addition of Tin(IV) *Chloride to a Mixture of Dimethyl Sulphoxide and Pyridine.*—The chloride (3·60 g., 1 mol.) in methylene chloride (10 ml.) was slowly added dropwise to a solution of the sulphoxide (5·00 g., 4·9 mol.) and pyridine (5·00 g., 4·6 mol.) in the same solvent (20 ml.) at 0°. Reaction was vigorous and the white solid tin(IV) chloride–dipyridine complex (5·60 g., 95%) (Found: Cl, 34·1; C_5H_5N, 35·7. Calc. for $C_{10}H_{10}Cl_4N_2Sn$: Cl, 34·0; C_5H_5N, 37·8%) was instantly precipitated, filtered off, washed with methylene chloride, and freed from solvent at 20°/10 mm. The identity of the complex was confirmed by comparison of its infrared spectrum with that of an authentic sample.

Infrared Spectra of the Complexes.—In Table 5 are shown the results necessary to supplement Table 2 and Figs. 1 and 2. The spectra of the four sulphoxides, and one complex for each, are either reproduced [Ph_2SO and $(Ph_2SO)_2,SnCl_4$] or described.

We thank Drs. T. Colclough and D. A. Spratt for samples of sulphoxides, Dr. Colclough, Dr. G. Holt, and Professor N. Kharasch for helpful discussions, and the D.S.I.R. for a personal grant (to J. K. S.).

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634. *Trigallic Acid, A Probable Component of Tannic Acid.*

By H. G. C. King and T. White.

A component of tannic acid is believed to be *m*-trigallic acid. Its isolation and properties are described, and an apparently identical product is synthesised.

"Tannic acid" is a mixture,[1] three of whose main components are acidic and can be separated from the classical gallotannin by extraction with solvent from a neutralised solution of "tannic acid."[2] Two of the acidic components are gallic and *m*-digallic acid and it was suggested that the third was a trigallic acid (*a*) by reason of its position on paper chromatograms and (*b*) since brief acid hydrolysis of purified gallotannin produced gallic acid, *m*-digallic acid, and component **3**. Prolonged hydrolysis destroyed component **3** and *m*-digallic acid in that order, the sole product from each being then gallic acid.

Component **3** has since been isolated by chromatographing the mixture of acids on a column of "Solka Floc" powdered cellulose. For comparison, a synthetic trigallic acid was made by condensing penta-*O*-acetyl-*p*-digalloyl chloride with 3,5-di-*O*-acetylgallic acid, then simultaneously deacetylating and rearranging the resulting hepta-acetyl derivative.

The synthetic and the natural product each crystallise from water with two molecules of water of crystallisation. They appear to have identical paper chromatographic and ultraviolet spectrophotometric properties, and elementary analyses are satisfactory, but the synthetic sample has a lower melting point although the mixed melting point is intermediate. Total acid hydrolysis of both acids produced gallic acid in about the expected molecular ratio, as found by measurements of ultraviolet spectra;[3] molecular-weight and equivalent-weight determinations for the synthetic product gave values of the right order.

Both the synthetic and the natural product are believed to be *m*-trigallic acids since alkaline hydrolysis of the methylation product yielded only 3,4-di- and 3,4,5-tri-*O*-methylgallic acid. The initial methylations were intended to produce the methyl ester of fully methylated trigallic acid but in each case the product had too high a methoxyl content. Independent work on corresponding structures at the University of Sheffield[4] suggests that methylation with diazomethane caused methanolysis of the parent acids, yielding mixtures of methyl tri- and di-*O*-methylgallate.

Determination of the *ortho*-hydroxyl value of the synthetic acid by the ferrous tartrate method[3] supported the formulation as a *m*-galloyl-*m*-digallic acid. The compound behaved as a galloyl ester, giving a value of 68·6% of pyrogalloyl-type groups (calc. 72·2%).

Neither the occurrence nor the synthesis of a *m*-galloyl-*m*-digallic acid has been reported previously. Fischer and Freudenberg[5] synthesised a trigallic acid by treating tri-*O*-methoxygalloyl chloride with gallic acid, but gave it the structure 3,5-digalloylgallic acid. The demonstration of the presence of a trigallic acid residue in the gallotannin molecule is, of course, of some importance.

Experimental

Synthesis of Trigallic Acid.—Hepta-O-acetyltrigallic acid. Penta-*O*-acetyl-*p*-digallic acid (7·5 g.) was made into a slurry in carbon tetrachloride (22·5 ml.), and phosphorus pentachloride (7·5 g.) was added in small portions. The mixture was warmed on a water-bath until dissolution took place. The excess of pentachloride was removed by filtration through glass wool.

[1] White, Kirby, and Knowles, *J. Soc. Leather Trades' Chemists*, 1952, **36**, 148.
[2] King, Ph.D. Thesis, London, 1957.
[3] King and White, "Symposium on Chemistry of Vegetable Tannins," Society of Leather Trades' Chemists, Croydon, 1956.
[4] Professor R. D. Haworth, personal communication.
[5] Fischer and Freudenberg, *Ber.*, 1912, **45**, 2709.

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The acid chloride crystallised overnight at 0°. The cream-coloured product, re-crystallised from carbon tetrachloride, had m. p. 150° (3·5 g., dried at 76° over P_2O_5 in a vacuum).

3,5-Di-*O*-acetylgallic acid (1·75 g.) in acetone (10 ml.) was cooled to −5° with stirring and aqueous N-sodium hydroxide (6·5 ml.) was added. Penta-*O*-acetyl-*p*-galloyl chloride (3·5 g.) in acetone (3 ml.) was added with simultaneous additions of N-sodium hydroxide (1·3 ml.). The purple solution formed was acidified to Congo Red with dilute hydrochloric acid, yielding a brown oil. Water (25 ml.) was added and the oil rubbed until it solidified. The cream-coloured plastic product had m. p. 142° (decomp.) (3·6 g., dried at 100° over P_2O_5 in a vacuum).

Trigallic acid. To a slurry of hepta-*O*-acetyltrigallic acid (2·5 g.) in water (10 ml.) at −5° under hydrogen, 5N-ammonia was added dropwise until the solid dissolved. The pink solution was kept for 1 hr. at room temperature, then acidified to Congo Red paper and kept at 0° overnight. The white precipitate of ***trigallic acid*** was filtered off, washed with chloroform, allowed to dry, and washed again with cold water (yield, 1·39 g., dried at 100° as above), then having m. p. 213° (decomp.) after softening at 170°. The product was recrystallised from water, giving an acid showing no other components on two-way paper chromatography [R_F 0·13 in 6% acetic acid, 0·81 in butan-2-ol–acetic acid–water (14 : 1 : 5)] and having m. p. 217° (decomp.) after softening at 192° (Found: C, 49·2; H, 3·5; loss in wt. at 140°/0·1 mm., 6·7. Calc. for $C_{21}H_{14}O_{13},2H_2O$: C, 49·3; H, 3·5; H_2O, 7·6%).

The ultraviolet spectrum of the product in ethanol showed a single maximum at 270 mμ ($E^{1\%}_{1\,cm.}$ 598), minimum at 240 mμ ($E^{1\%}_{1\,cm.}$ 263). Hydrolysis by 2N-sulphuric acid (2 ml.) of this material (2·52 mg.) was carried out for 16 hr. at 100°. The volume of solution was made up to 100 ml. with water. Two-dimensional paper chromatography of the solution showed the presence of a single component, gallic acid, whose ultraviolet spectrum showed a maximum at 270 mμ ($E^{1\%}_{1\,cm.}$ 570). The corresponding $E^{1\%}_{1\,cm.}$ value for gallic acid treated as above was 552 at the same wavelength.[3]

The *ortho*-di- and tri-hydroxyl content of trigallic acid [3] was determined by the ferrous tartrate method as follows: Trigallic acid (26·85 mg.) was dissolved in a mixture of ethanol (5 ml.) and water (45 ml.), and 10 ml. aliquot parts were developed with the buffered ferrous tartrate reagent, measurements being made at 545 mμ. The E value between borate and acetate buffer readings was negligible, indicating that the compound was behaving as a galloyl ester (*m*-digallic acid type). The analytical result was 68·6% of pyrogallol-type groups (calc. for a 4,4′-digalloylgallic acid, 26·5%; for a 3,5-digalloylgallic acid, 52·8%; for a 3,3′-digalloylgallic acid, 72·2%).

Molecular weight determinations were carried out for acetone solutions by the ebullioscopic method of Bobranski and Sucharda, checked against *m*-digallic acid. These gave: *m*-digallic, M 320 (calc., 328); trigallic acid, M 483, 498 (calc., 474).

Equivalent-weight determinations were carried out by potentiometric titration in 1 : 1 ethylene glycol–butan-1-ol with 0·161N-potassium hydroxide in the same solvent mixture. Determinations on gallic and *m*-digallic acids were used as control. Results are of the order expected if the product is made up of 3 galloyl residues, namely: gallic (hydrate), 188 (calc., 185); *m*-digallic, 322 (calc., 343); trigallic acid, 474 (calc., 441).

Methylation of trigallic acid. Trigallic acid (0·53 g.) was treated in methanol (5 ml.) and ether (25 ml.) with an excess of ethereal diazomethane, then kept at room temperature for 3 days, after which the solvent was distilled off. The residual syrup was heated with 50% aqueous methanol (10 ml.) and the irregular shaped crystals which separated on cooling were filtered off (0·46 g., dried at room temperature over P_2O_5 in a vacuum). Recrystallisation from methanol gave a derivative, m. p. 100° (the product required several days to solidify, first separating as an oil) [Found: C, 58·8; H, 5·1; OMe, 54·0. Calc. for $C_{21}H_8O_5(OMe)_6$: C, 59·5; H, 5·1; OMe, 42·3%]. The high methoxyl content suggests that the product is a mixture of methyl tri- and di-*O*-methylgallic acid found in the next experiment and produced by methanolysis of the parent substance.

Alkaline hydrolysis of the product of methylating trigallic acid. The methylation product (0·32 g.) was kept in methanol (10 ml.) and 10% aqueous sodium hydroxide (5 ml.) for 6 hr. at 40° in an atmosphere of nitrogen, then at room temperature overnight, and was acidified with 6N-hydrochloric acid. The methanol was partly distilled off and the crystalline product (crop 1) was filtered off and dried over P_2O_5 (vacuum) (yield, 0·09 g.; m. p. 145—150°). The mother-liquors were concentrated to 15 ml., further crystals being obtained (0·06 g., dried as above; m. p. 168—183°) (crop 2). Crop 2 was washed with 1 : 1 chloroform–carbon tetrachloride

(4 ml.), leaving 3,4-di-*O*-methylgallic acid which, recrystallised from water, had m. p. and mixed m. p. 187°.

The chloroform–carbon tetrachloride-soluble portion was mixed with crop 1 (soluble in the mixture), and the solvents were allowed to evaporate. The residue recrystallised from water, giving needles of 3,4,5-tri-*O*-methylgallic acid, m. p. and mixed m. p. 163°.

These results were confirmed by repeating the hydrolysis and chromatographing the acidified hydrolysate one-way on paper with butan-1-ol saturated with aqueous formic acid as solvent. Both the di- and the tri-*O*-methylgallic acid were located by a faint violet fluorescence when exposed to ammonia vapour and ultraviolet light, and by their faint yellow reactions when the chromatograms were sprayed with bisdiazotised benzidine. R_F values were: 3,4,5-tri-*O*-methylgallic acid, 0·84; 3,4-di-*O*-methylgallic acid, 0·77. Both acids reacted positively to the Bromophenol Blue indicator spray. There was no sign of 3,5-di-*O*-methylgallic or 4-*O*-methylgallic acid on these chromatograms.

Acetyl derivative of trigallic acid. Trigallic acid (100 mg.) was kept in pyridine (10·5 ml.) with acetic anhydride (5 ml.) for 2 days at room temperature, and then poured into water (50 ml.) containing 10% w/v sulphuric acid (1 ml.). The sticky product was allowed to harden and was then filtered off (136 mg., dried at 76° as above). The derivative recrystallised from dilute acetic acid, giving a *product*, m. p. 175°, softening at 125—130° [Found: C, 54·1; H, 3·7; OAc, 39·6. Calc. for $C_{21}H_7O_8(OAc)_7$: C, 54·8; H, 3·6; OAc = 39·3%].

Preparation of Component 3 from Tannic Acid.—Tannic acid (80 g.) was dissolved in water (400 ml.), and the solution adjusted to pH 6·5 with sodium hydrogen carbonate (about 20 g.) and then extracted with ethyl acetate (2 × 150 ml.; 4 × 100 ml.). The combined extracts were dried (Na_2SO_4) and taken to dryness (yield, 44·2 g., mainly gallotannin). Dilute hydrochloric acid was added to the aqueous residue, to give pH 2, and the solution was extracted exhaustively with ether. The extract was dried and taken to dryness, giving material (20·2 g.), predominantly a mixture of gallic and *m*-digallic acid and component 3, with a little gallotannin. The extract was dissolved in hot water (40 ml.) and allowed to cool. A white precipitate separated; this was recrystallised from water (40 ml.) (yield, 6·4 g., air-dry; mainly *m*-digallic acid with a little gallic acid and component 3). The mother-liquors were combined and taken to dryness (13 g.), the residue was dissolved in water (150 ml.), and the solution adjusted to pH 6·5 and again extracted with ethyl acetate to remove gallotannin. The aqueous residue was re-adjusted to pH 2 and extracted exhaustively with ether, the extract yielding gallic acid, *m*-digallic acid, and component 3 uncontaminated with gallotannin.

The acidic fraction (1 g.) was dissolved in the minimum amount of 5% acetic acid and applied to a " Solka Floc " column (47 × 3·5 cm.), the column being developed with 5% acetic acid. Samples (10 ml.) were collected as soon as the effluent reacted with the ferric chloride–potassium ferricyanide reagent, the type of acid present in each sample being checked by one-way paper chromatography (6% acetic acid). Fractions 1—12 contained gallic acid and fractions 13—57 *m*-digallic acid. The latter fractions were reduced to a small volume with repeated additions of water to remove acetic acid. *m*-Digallic acid (0·4 g.), m. p. 254°, crystallised. When paper-chromatographic checks showed that only component 3 was emerging, 24 × 10 ml. and 4 × 50 ml. samples were collected. The effluent reacted only very faintly with the ferricyanide reagent when the last sample had been collected. The fractions were combined and their volumes reduced by vacuum-distillation as before at a water-bath temperature of 50°. When the volume had been reduced to 10 ml. the precipitated component 3 was filtered off, washed with water, and dried at 75° as before [75 mg.; m. p. 226° (decomp.)]. Recrystallisation of component 3 from water raised the m. p. to 237° (decomp.), mixed m. p. with synthetic trigallic acid 222° (decomp.) (Found: C, 49·2; H, 3·5; loss in wt., 7·1. Calc. for $C_{21}H_{14}O_{13}.2H_2O$: C, 49·3; H, 3·5; H_2O, 7·6%). Hydrolysis by 2N-sulphuric acid (2 ml.) of component 3 (2·95 mg.) gave gallic acid as the sole product, $E^{1\%}_{1\,cm.}$ 545 at 270 mμ.[3] Its behaviour on paper chromatograms was identical with that of the synthetic trigallic acid.

Methylation. Component 3 (50 mg.) was dissolved in the minimum amount of methanol, and ether (20 ml.) was added. Excess of ethereal diazomethane solution was added and the solution left at room temperature overnight. The ether was distilled off and the remaining methanolic residue was kept at 0° until crystallisation occurred. The product (40 mg., dried at room temperature as above) had m. p. 112° [Found: C, 59·1; H, 4·8. Calc. for $C_{21}H_6O_5(OMe)_8$: C, 59·5; H, 5·1%]. Methoxyl values were too high, as already explained.

Acetate. Component 3 (100 mg.) was warmed with pyridine (0·5 ml.) and acetic anhydride

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(5 ml.) until dissolved. The solution was left overnight at room temperature and, after filtration, was poured into 3·7% hydrochloric acid (50 ml.). After solidification, the acetyl derivative was filtered off and dried at room temperature over P_2O_5 in a vacuum; it (110 mg.) had m. p. 175° after softening at 125—130°, mixed m. p. with synthetic hepta-acetyltrigallic acid, 175°, softening at 125—130° [Found: C, 53·5; H, 4·0; OAc, 38·0. Calc. for $C_{21}H_7O_6(OAc)_7$: C, 54·8; H, 3·6; OAc, 39·3%].

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635. *The Occurrence of* 2-*Benzyl*-2-*hydroxycoumaran*-3-*ones in Quebracho Tannin Extract.*

By H. G. C. KING, T. WHITE, and (in part) R. B. HUGHES.

The isolation and identification of the crystalline 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one from commercial Quebracho tannin extract is now detailed. The structure of the compound has been confirmed by dehydration to the corresponding benzylidenecoumaran-3-one (aurone) and by synthesis from ω-hydroxyresacetophenone and isovanillin.

2-Benzyl-2,6,3′,4′-tetrahydroxycoumaran-3-one is also present in the above tannin but was less amenable to investigation.

THE existence of two 2-benzyl-2-hydroxycoumaran-3-ones in Quebracho tannin extract (the aqueous heartwood extract of *Schinopsis balansae* and *S. lorentzii*) has been announced [1,2] and throws new light on the biogenetic relations of C_6–C_3–C_6 compounds. The family Anacardiaceae is remarkable for the occurrence in species of the *Schinopsis* and *Rhus* genera of biogenetically related compounds having a common hydroxylation pattern and differing only in the state of oxidation of the central ring. These are fisetin (3,7,3′,4′-tetrahydroxyflavone) from Quebracho extract,[3] which also contains 4-methoxyfisetin, 3,7,4′-trihydroxyflavone, and 3,7,3′,4′,5′-pentahydroxyflavone (robinetin);[4] also fustin (3,7,3′,4′-tetrahydroxyflavanone) from the heartwood of *Rhus succedanea*,[5] sulphuretin (6,3′,4′-trihydroxyaurone) from the wood of *Rhus cotinus*,[1] and leucofisetinidin (3,4,7,3′,4′-pentahydroxyflavan) from *Schinopsis balansae* and *S. lorentzii*.[1] * The present 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one (and the 2,6,3′,4′-tetrahydroxy-analogue) has a similar overall hydroxylation pattern; the 4′-methoxy-group is comparatively rare in Nature but has already been recorded [4] for Quebracho in the case of 3,7,3′-trihydroxy-4′-methoxyflavone. In no other botanical family have so many C_{15} compounds of identical hydroxylation pattern been isolated although in several cases two components occur, differing only in the oxidation level of the C_3 portion.

The structural relations between the various flavonoid compounds mentioned above is shown in the following scheme, the arrows indicating known conversions *in vitro*.

* This observation was announced by the present authors [1,2] in 1957 despite absence of reference to it in later communications.[6]

[1] King and White, *Proc. Chem. Soc.*, 1957, 341.
[2] King and White, *J. Soc. Leather Trades' Chemists*, 1957, **41**, 368.
[3] Perkin and Gunnel, *J.*, 1896, **69**, 1304.
[4] Kirby and White, *Biochem. J.*, 1955, **60**, 582.
[5] Oyamada, *Annalen*, 1939, **538**, 44.
[6] Roux, *Chem. and Ind.*, 1958, 161; Freudenberg and Weinges, *Annalen*, 1958, **613**, 61; Weinges, *ibid.*, 1958, **615**, 203; Roux and Evelyn, *Biochem. J.*, 1958, **69**, 530.

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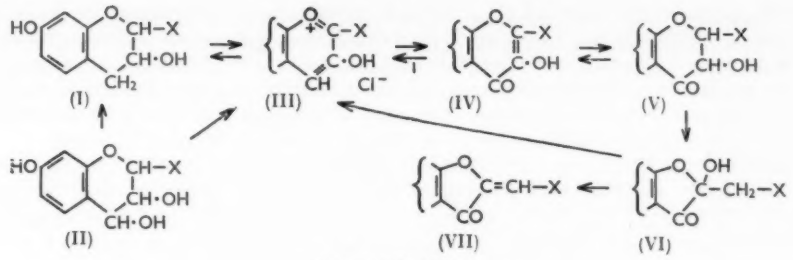

X = 3,4-$(HO)_2C_6H_3$.

(I) Flavanol. (II) Leucoanthocyanidin. (III) Anthocyanidin. (IV) Flavonol. (V) Dihydroflavonol. (VI) 2-Benzyl-2-hydroxycoumaran-3-one. (VII) Aurone.

I, *Via* the reduced acetate.

The general reactivity of the hydroxylated 2-benzylcoumaran-3-ones resembles that of the catechins and leucoanthocyanidins and this new group of polyphenols must, therefore, enter into considerations of the nature of the precursors of the condensed tannins. The synthesis and characterisation of the examples now recorded in Quebracho extract presented particular difficulties, mainly because recorded work on substances of this type has concerned examples lacking hydroxyl groups other than in the 2-position, or possessing a 4-hydroxyl group capable of hydrogen-bonding with the 3-keto-group, factors which affect considerably the reactivity and ease of synthesis of these substances.

2-Benzyl-2-hydroxycoumaran-3-ones have been suggested [7] as intermediates in the synthesis of aurones from dihydroflavanols. 2-Benzyl-2-hydroxycoumaran-3-one itself resulted when Gripenberg [8] treated 3-hydroxyflavanone with alcoholic potassium hydroxide and he identified as 2-benzyl-2-hydroxy-4,6-dimethoxycoumaran-3-one the " apoalpinone monomethyl ether " similarly obtained by Lindstedt [9] from pinobanksin dimethyl ether (3-hydroxy-5,7-dimethoxyflavanone). Zwingelstein and Jouanneteau [10] used aqueous alkali to convert quercetin into 2-benzyl-2,4,6,3′,4′-pentahydroxycoumaran-3-one. We applied these techniques to fisetin but obtained no 2-benzyl-2,6,3′,4′-tetrahydroxycoumaran-3-one, presumably because of the absence of a 5-hydroxyl group and presence of other reactive hydroxyl groups in fisetin. With a view to obtaining the 2-benzyl-4′-methoxy-compound we attempted to convert 4′-methoxyfisetin first into the corresponding flavanone by treatment with sodium dithionite,[11] but again the reaction failed, as it did also with fisetin (again absence of 5-hydroxyl group since substances with this group are converted readily into dihydro-derivatives).

However, the required fustin (3,7,3′,4′-tetrahydroxyflavanone) occurs naturally and was synthesised by treating 3,4,2′,4′-tetrahydroxychalcone with alkaline hydrogen peroxide under conditions used by Anand *et al.*[12] Boiling alcoholic potassium hydroxide converted it into a complex mixture containing very small amounts of the required 2-benzyl-2,6,3′,4′-tetrahydroxycoumaran-3-one. Curiously, when Jouanneteau *et al.*[13] applied a similar treatment to taxifolin (dihydroquercetin) the product had no 2-hydroxyl group but was 2-benzyl-4,6,3′,4′-tetrahydroxycoumaran-3-one.

An alternative approach is to treat α-hydroxy- or α-methoxy-chalcones with mineral acid. Gripenberg [8] thus obtained 2-benzyl-2-hydroxycoumaran-3-one from 2′-hydroxy-α-methoxychalcone, and Enebäck and Gripenberg [14] synthesised 2-benzyl-2-methoxycoumaran-3-one

[7] Molhs, Coillard, and Mentzner, *Bull. Soc. chim. France*, 1954, 1397.
[8] Gripenberg, *Acta Chem. Scand.*, 1950, **4**, 1323.
[9] Lindstedt, *Acta Chem. Scand.*, 1950, **4**, 772.
[10] Zwingelstein and Jouanneteau, *Compt. rend.*, 1955, **240**, 981.
[11] Pew, *J. Amer. Chem. Soc.*, 1948, **70**, 3031.
[12] Anand, Iyer, and Venkataraman, *Proc. Indian Acad. Sci.*, 1949, **29**, *A*, 203.
[13] Jouanneteau, Zwingelstein, and Mentzner, *Compt. rend.*, 1954, **239**, 1514.
[14] Enebäck and Gripenberg, *Acta Chem. Scand.*, 1957, **11**, 866.

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from the same source although they failed to obtain it by methylating its 2-hydroxy-analogue. Tsukamoto and Tominaga [15] later established that certain α-methoxychalcones can be converted simultaneously into 2-benzyl-2-hydroxy- and -2-methoxy-coumaranones, but our treatment of 3,2′,4′-trihydroxy-α,4-dimethoxychalcone with acid gave only a dimethoxy-derivative * (ultraviolet spectrum almost identical with that of 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one), no 2-hydroxy-analogue being obtained.

Using Saiyad, Nadkarni, and Wheeler's method [16] for the synthesis of chalcones we then condensed ω-hydroxyresacetophenone with isovanillin in the presence of aqueous potassium hydroxide: we obtained, among other products, 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one directly; the expected α-hydroxychalcone is presumably unstable and rearranges immediately. The synthesis, although unexpected, served to establish finally the identity of the crystalline product from Quebracho extract,[1,2] this being the first record of the existence in Nature of compounds of this general structure.†

2-Benzyl-2-hydroxycoumaranones in Quebracho.—Two compounds resulted when the acetone-soluble portion of Quebracho extract was extracted with ether, and the water-soluble portion of this ether extract chromatographed on powdered-cellulose columns with dilute acetic acid as eluant. Neither the acetates not the methoxy-derivatives crystallised but the general structures became clear when treatment with concentrated sulphuric acid converted one into the aurone sulphuretin, and the other into 6,3′-dihydroxy-4′-methoxyaurone. Both this and its parent 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one gave a bright scarlet colour when dissolved in glacial acetic acid containing a trace of sulphuric acid, a reaction found to have structural significance.[18] Further evidence for the general structure is that treatment of the reduced acetate of 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one with hot propan-2-ol–hydrogen chloride [19] gave the same anthocyanidin as did the reduced acetate of fisetin 4′-methyl ether under the same conditions.

Experimental

Isolation of 2-Benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one.—Quebracho extract (1·5 kg.), dried in a vacuum over P_2O_5, was shaken with dry acetone (2 l.) for 24 hr., and the solution centrifuged off. This process was twice repeated. The combined extracts were concentrated to s.g. 0·975 and stirred with an equal volume of ether. The next morning the solution was decanted and taken to dryness; the residue was redissolved in acetone to a solution of s.g. 0·975 and again treated with ether (2 l.). After being kept overnight the solution was removed and taken to dryness. This product (110 g.) was dissolved in water (750 ml.) and extracted continuously with ether until the extract was colourless. The ether extract was taken to dryness and the product (15 g.) dissolved in warm 5% acetic acid (30 ml.). The flavonoid material which separated on cooling was filtered off and the filtrate chromatographed on a column of " Solka Floc " (30″ × 2″) with 5% acetic acid as the solvent. When the effluent reacted with the ferricyanide or diazotised benzidine polyphenol reagent,[20] samples (15 ml.) were collected and refrigerated overnight. 2-Benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one separated as clumps of white crystals in several successive tubes, usually nos. 6—12. A spot of solution from each tube was chromatographed on paper in 6% acetic acid and examined in ultraviolet light after being sprayed with the benzidine reagent. This showed the presence of the coumaranone up to tube 14, accompanied by the closely related 2-benzyl-2,6,3′,4′-tetrahydroxycoumaran-3-one. The crystals were filtered off and the filtrates and contents of the remaining tubes known to contain the benzylcoumaranones were concentrated, thus yielding

* R. A. Low synthesised the same dimethoxy-derivative at Sheffield University.

† Jones, King, and Morgan [17] have since observed a 2-benzyl-2-hydroxycoumaran-3-one in *M. eminii* wood.

[15] Tsukamoto and Tominaga, *J. Pharm. Soc. Japan*, 1953, **73**, 1172.
[16] Saiyad, Nadkarni, and Wheeler, *J.*, 1937, 1737.
[17] Jones, King, and Morgan, *Chem. and Ind.*, 1961, 346.
[18] King and White, *J.*, 1961, 3539.
[19] King and White, *J.*, 1957, 3901.
[20] White, Kirby, and Knowles, *J. Soc. Leather Trades' Chemists*, 1952, **36**, 148.

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a further small quantity of crystalline trihydroxy-4′-methoxy-compound. The concentrated filtrate from this, containing the crude tetrahydroxy-compound, was set aside for later work. The yield of *2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one* in typical experiments was 0·3 g. (0·02% on the wt. of extract taken); recrystallised from water this product formed white needles, m. p. 194° (Found: C, 63·6; H, 4·6; OMe, 10·1. $C_{15}H_{11}O_4$·OMe requires C, 63·7; H, 4·6; OMe, 10·3%). It gave a red-brown colour with aqueous ferric chloride solution. Fusion with potassium hydroxide produced resorcinol, guaiacol, and protocatechuic acid (under these conditions isovanillic was demethylated to protocatechuic acid). Its R_F on paper chromatograms in 6% acetic acid was 0·74 and in 14 : 1 : 5 butan-2-ol–acetic acid–water was 0·94. Under ultraviolet light the spot is dark; it becomes violet in ammonia vapour. The compound has $\lambda_{max.}$ 232, 278, and 325 mμ ($E^{1\%}_{1\,cm.}$ 482, 505, and 293).

The *triacetate* (obtained in pyridine–acetic anhydride) was a glass, flowing at 147° [Found: OAc, 31·2; OMe, 7·6. $C_{15}H_9O(O{\cdot}CO{\cdot}CH_3)_3$·OMe requires Ac, 30·2; OMe, 7·3%], unchanged in methoxyl content on treatment with diazomethane.

The parent 2-benzylcoumaran-3-one with (*a*) diazomethane, (*b*) dimethyl sulphate and alkali, or (*c*) diazomethane after treatment (*b*) gave a *trimethyl ether* [Found: OMe, 28·5. $C_{15}H_9O_3(OMe)_3$ requires OMe, 29·1%], one hydroxyl group being unmethylated.

2-Benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one dissolved readily in sodium hydrogen carbonate solution and was recovered unchanged on acidification. It could be titrated directly with sodium hydroxide, giving an equivalent weight of 300 (calc., 302), but the methylation experiments prove the absence of carboxyl and lactone groups. The presence and position of a tertiary hydroxyl and of the 4′-methoxyl group followed from dehydration of the compound with sulphuric acid to an aurone (see below).

Adding a drop of concentrated sulphuric acid to a very dilute solution of the coumaran-3-one or its related aurone in acetic anhydride produced a bright red colour.[18] In the former case, the normal triacetate was formed together with the aurone diacetate which resulted from simultaneous acetylation and dehydration. The aurone gave only its own diacetate. The two acetates are readily separated and demonstrated on paper chromatograms run in 25% acetic acid and sprayed with 5% aqueous sodium hydroxide as they show up as yellow spots. The R_F values were: coumaran-3-one triacetate 0·97; aurone diacetate 0·71.

Isolation of 2-Benzyl-2,6,3′,4′-tetrahydroxycoumaran-3-one.—50 ml. of final concentrated filtrate from several isolations of 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one from Quebracho extract were chromatographed with 5% acetic acid on a " Solka Floc " column; the effluent was collected until paper chromatograms showed that all the tetrahydroxycoumaranone had been eluted. The part of the effluent containing this product was extracted exhaustively with ether, the extract dried, and the ether distilled off, yielding a brown glass (7·08 g.). Paper chromatography showed the presence of some gallic acid and some trihydroxy-4′-methoxycoumaranone. The product was dissolved in 2% aqueous sodium hydrogen carbonate (100 ml.) and extracted with ethyl acetate. The extract was concentrated to a glass which was dissolved in water (200 ml.) and treated with saturated (normal) lead acetate solution to precipitate the tetrahydroxycoumaranone. The precipitate was filtered off, washed with water, resuspended in water, and brought to pH 1·5 with 10% w/v sulphuric acid to remove lead as sulphate. After filtration, extraction with ethyl acetate followed by removal of the solvent left an orange-brown hygroscopic solid consisting of 2-benzyl-2,6,3′,4′-tetrahydroxycoumaran-3-one (1·913 g.) with a trace of flavanoid material. The substance is oxidised very readily in solution and it was not possible to crystallise or purify it further. It is very soluble in water, alcohol, and ether and melted at 105°. Ferric chloride solution produced a green colour. Dehydration with sulphuric acid produced the corresponding aurone, sulphuretin; treatment with sulphuric acid in acetic anhydride gave a mixture of the tetra-acetate of the coumaranone and of sulphuretin triacetate. These were again readily separated and detected on paper chromatograms run in 25% acetic acid and had R_F 0·91 (coumaranone tetra-acetate) and 0·79 (sulphuretin triacetate). Acetylation and methylation gave only glasses.

6,3′-Dihydroxy-4′-methoxyaurone.—6-Hydroxycoumaran-3-one (4 g.) was condensed with isovanillin (4 g.) for 30 min. with ethanol (300 ml.) and concentrated hydrochloric acid (200 ml.), then poured into water (2·5 l.). The resultant sticky product was filtered off and dissolved in the minimum volume of acetone, and the solution concentrated by distillation until the *aurone* separated (4·3 g.; m. p. 230°). It recrystallised from methanol as yellow needles, m. p. 254° (Found: C, 68·1; H, 4·2; OMe, 11·7. $C_{15}H_9O_4$·OMe requires C, 67·8; H, 4·2; OMe, 11·0%).

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On paper chromatograms spots fluoresce yellow-green under ultraviolet light, the colour changing to light green in ammonia vapour. Its R_F in acetic acid–water–hydrochloric acid (30 : 15 : 1) [21] is 0·76, and in butan-2-ol–acetic acid–water (14 : 1 : 5) is 0·92.

Formation of 6,3′-*Dihydroxy*-4′-*methoxyaurone from* 2-*Benzyl*-2,6,3′-*trihydroxy*-4′-*methoxycoumaran*-3-*one*.—The coumaranone (0·5 g.) was dissolved in ice-cold concentrated sulphuric acid (10 ml.), and after exactly 8 min. was poured on crushed ice (100 g.). The initial orange precipitate quickly redissolved, leaving a clear golden-yellow solution which was extracted with ethyl acetate. The extract was dried and concentrated to 1 ml., then water (50 ml.) was added and residual sulphuric acid removed by stirring with Deacidite E ion-exchange resin. The deionised solution was taken to dryness (yield 84 mg.). Paper chromatography in aqueous acetic–hydrochloric acid (see above) against synthetic 6,3′-dihydroxy-4′-methoxyaurone showed this product to be present (R_F 0·73) and also a substance (R_F 0·80) fluorescing yellow in ultraviolet light, a little sulphuretin (R_F 0·55), and some unchanged starting material (R_F 1·00). Recrystallising the crude product from ethanol–water produced pure 6,3′-dihydroxy-4′-methoxyaurone identical in chromatographic behaviour, spectrum, and decomposition temperature (238—240°) with the synthetic product.

6,3′-*Dihydroxy*-4′-*methoxyauronesulphonic Acid*.—(*a*) Aurone (1 g.) was dissolved in warm concentrated sulphuric acid (20 ml.), and the deep red solution cooled and poured into water (250 ml.). The orange precipitate soon redissolved and the solution was then passed down a column of " Solka Floc " cellulose (26 × 2 in.) previously set up with water; development was with water. The mobile orange-brown band of sulphonated aurone was collected and its volume reduced to 50 ml., yielding a red-orange solid (0·8 g.) which recrystallised from water as orange needles and after drying *in vacuo* had m. p. 258° (decomp.), $\lambda_{max.}$ 250 ($E^{1\%}_{1cm.}$ 406) and 380 mμ ($E^{1\%}_{1cm.}$ 662). Potentiometric titration of the sulphonated aurone gave an equivalent weight of 360, corresponding to 1 HSO_3 group. The acid formed an S-*benzylthiouronium salt*, m. p. 207° (from 50% aqueous alcohol) (Found: C, 51·9; H, 4·7; S, 11·4; OMe, 5·8. $C_{22}H_{19}N_2O_7S_2$·OMe,H_2O requires C, 51·7; H, 4·5; S, 11·9; OMe, 5·8%).

(*b*) 2-Benzyl-2,6,3′-trihydroxy-4′-methoxycoumarone, treated as in (*a*), gave a similar acid (of lower m. p.) affording the same salt.

6,3′-*Diacetyl*-4′-*methoxyaurone*.—6,3′-Dihydroxy-4′-methoxyaurone (0·25 g.) with acetic anhydride (10 ml.) and concentrated sulphuric acid or acetic anhydride (2 drops) and sodium acetate gave the diacetate, m. p. 165° (0·2 g.).

6,3′,4′-*Triacetylaurone* (*Sulphuretin Triacetate*).—Sulphuretin (0·25 g.) was converted into its triacetate, m. p. 167°, by preceding methods.

Formation of 6,3′-*Diacetyl*-4′-*methoxyaurone and* 2-*Benzyl*-2,6,3′-*triacetyl*-4′-*methoxycoumaran*-3-*one from* 2-*Benzyl*-2,6,3′-*trihydroxy*-4′-*methoxycoumaran*-3-*one*.—The trihydroxycoumaranone (0·23 g.) was treated with acetic anhydride (10 ml.) containing concentrated sulphuric acid (0·025 ml., the proportion giving the maximum colour). The product (0·28 g.) melted from 80° to 133° and decomposed at 155—160°. Paper chromatography showed that it was a mixture of 6,3′-diacetyl-4′-methoxyaurone and 2-benzyl-2,6,3′-triacetyl-4′-methoxycoumaran-3-one, and slow crystallisation from ethanol gave needles of the aurone, m. p. 161°. The mixed acetates (0·5 g.) were boiled with N-ethanolic potassium hydroxide (5 ml.) for 5 min. A brown product separated during several days and was filtered off and dried (0·17 g.). Paper chromatography in acetic acid–water–hydrochloric acid (30 : 15 : 1) showed it to be 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one with 6,3′-dihydroxy-4′-methoxyaurone and a flavone-like material. This product was dissolved in 5% sodium hydroxide solution (10 ml.) and acidified with hydrochloric acid, and a brown precipitate was filtered off. The filtrate deposited further material on refrigeration for 3 days, this containing only the aurone and coumaranone. The latter was removed by boiling water, leaving pure 6,3′-dihydroxy-4′-methoxyaurone (65 mg.). The filtrate was taken to dryness and the residue extracted with ethanol, the extract yielding 62 mg. of product. This product was chromatographed on a " Solka Floc " column under the conditions used in isolating the parent coumaranone from Quebracho extract; the appropriate portion of eluant gave crystalline 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one (54 mg.).

Treatment of 2-*Benzyl*-2,6,3′,4′-*tetrahydroxycoumaran*-3-*one with Acetic Anhydride and Sulphuric Acid*.—The tetrahydroxy-coumaranone (0·27 g.) was acetylated as above, the product dissolved in chloroform, and the extract dried and evaporated, giving a golden oil (0·34 g.). This

[21] Bate-Smith, *Biochem. J.*, 1954, **58**, 122.

was dissolved in ethanol (2 ml.) and gave pale yellow needles on refrigeration for 3 days. The crystals were filtered off and air-dried (16 mg.; m. p. 165°). They were sulphuretin triacetate but paper chromatography showed the presence of traces of contaminants. Deacetylation as above produced only sulphuretin.

ω-Hydroxyresactophenone (*Fisetol*).—The product prepared by the method of Karrer and Biedermann [22] crystallised from water as needles, m. p. 191° (Found: C, 56·9; H, 4·9. Calc. for $C_8H_8O_4$: C, 57·2; H, 4·8%).

Synthesis of 2-Benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one.—Fisetol (1·24 g.) and isovanillin (1·1 g.) in ethanol (10 ml.) were treated with potassium hydroxide (10 g.) in water (7 ml.) on a boiling-water bath for 10 min., kept overnight, and acidified with concentrated hydrochloric acid. A sticky product separated after 3 days' refrigeration; the supernatant liquid was distilled off and the residue was treated with small volumes of glacial acetic acid to extract the product from accompanying salt. Water was then added to the total extract until precipitation was imminent and the solution was then chromatographed on a column of " Solka Floc " cellulose (26 × 2 in.) with 5% acetic acid as the eluant. Sixty 15-ml. fractions were collected, a paper-chromatographic check showing the presence of 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one in tubes 25—35. The product crystallised during several days in tubes 26—30 and was filtered off. The filtrates were concentrated with the contents of tubes 25 and 31—35, yielding a further crop (total yield, 106 mg., 4·9%). The m. p. and mixed m. p. with the natural trihydroxycoumaranone was 194° (Found: C, 63·8; H, 4·5; OMe, 10·3. Calc. for $C_{15}H_{11}O_5$·OMe: C, 63·7; H, 4·6; OMe, 10·3%), and $\lambda_{max.}$ were 232 ($E^{1\%}_{1\,cm.}$ 457), 278 ($E^{1\%}_{1\,cm.}$ 480), and 325 mμ ($E^{1\%}_{1\,cm.}$ 275).

3,2′,4′-Trihydroxy-α,4-dimethoxychalcone.—ω-Methoxyresacetophenone (1·8 g.) was warmed with isovanillin (1·5 g.) in ethanol (2 ml.) until homogeneous. Potassium hydroxide (17 g.) in water (12 ml.) was added and the mixture heated on a boiling-water bath for 10 min., then kept overnight at room temperature, diluted with an equal volume of water, and acidified with 50% w/v hydrochloric acid. The resulting sticky brown mass was washed with hot water and recrystallised twice from aqueous methanol, giving the *chalcone* (0·52 g.), m. p. 153° [Found: C, 60·7; H, 5·6; OMe, 20·3; H_2O, 5·4. $C_{15}H_{10}O_4(OMe)_2,H_2O$ requires C, 61·0; H, 5·4; OMe, 18·6; H_2O 5·4%].

2-Benzyl-6,3′-dihydroxy-2,4′-dimethoxycoumaran-3-one.—3,2′,4′-Trihydroxy-α,4-dimethoxychalcone (0·81 g.) was refluxed in ethanol (100 ml.) containing 2N-sulphuric acid (20 ml.) for 27 hr. The solution was subjected to paper chromatography (6% acetic acid); spraying with bisdiazotised benzidine gave a red, R_F 0·74, and a yellow spot, R_F 0·79. Both spots absorbed ultraviolet light before spraying and became dark violet when exposed to ammonia vapour. The ethanol was distilled from the reaction mixture and the remaining aqueous solution extracted with ether. The combined extracts were extracted twice with N-sodium hydroxide (20 ml.). Acidification of the alkaline extract with dilute hydrochloric acid gave an oil mixed with solid. This mixture was boiled with charcoal in water, giving a solution which, during several days at 0°, deposited first a sticky solid and then white crystals (22 mg.), m. p. 153°, giving the red spot of R_F 0·79 [Found: C, 59·9; H, 5·6; OMe, 18·3; loss at 100°, 5·6. $C_{15}H_{10}O_4(OMe)_2,H_2O$ requires C, 61·0; H, 5·4; OMe, 18·6; H_2O, 5·4%], $\lambda_{max.}$ 226 ($E^{1\%}_{1\,cm.}$ 442), 230 ($E^{1\%}_{1\,cm.}$ 436), 282 ($E^{1\%}_{1\,cm.}$ 552), and 325 mμ ($E^{1\%}_{1\,cm.}$ 265). This *product* gave the same scarlet reaction as 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one with acetic anhydride and sulphuric acid, but less intensely. No product corresponding to the spot of R_F 0·74 was isolated.

Synthesis of 2-Benzyl-2,6,3′,4′-tetrahydroxycoumaran-3-one.—Fustin (0·1 g.) was refluxed for 10 min. in methanol (10 ml.) containing potassium hydroxide (1 g.). The solution was cooled and acidified and the methanol distilled off. The remaining aqueous suspension was extracted with ether (5 × 10 ml.) and the dried, filtered extracts were taken to dryness, giving a golden, amorphous, hygroscopic solid (61 mg.). This was shown by paper chromatography, alone and in conjunction with a natural sample, to contain a high proportion of the required 2-benzylcoumaranone and treatment of this product with sulphuric acid yielded sulphuretin.

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See also p. 3234.]
[*Received, January 18th*, 1961.]

[22] Karrer and Biedermann, *Helv. Chim. Acta*, 1927, **10**, 441.

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636. *Mechanism of Reactions in the Sugar Series. Part IV.* The Structure of the Carbonium Ions formed in the Acid-catalysed Solvolysis of Glucopyranosides.*

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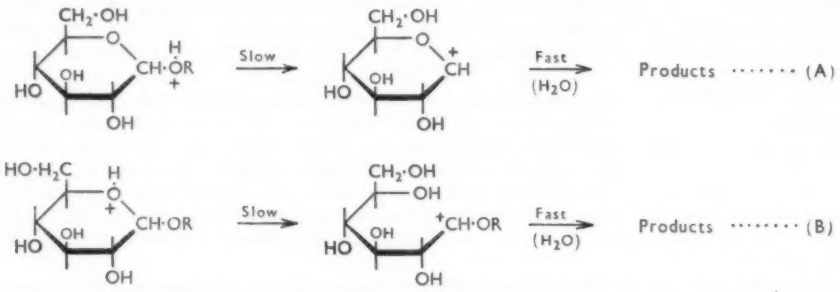
Acid-catalysed methanolysis of phenyl 2,3,4,6-tetra-*O*-methyl-β-D-glucopyranoside and of phenyl α- and β-D-glucopyranoside has been found to proceed with predominant inversion. *S*-Phenyl 2,3,4,6-tetra-*O*-methyl-β-D-thioglucopyranoside resists methanolysis in acidic solution. Acid-catalysed hydrolysis of methyl α-D-glucopyranoside is associated with an oxygen isotope effect. These results are consistent with the view that acid-catalysed solvolysis of D-glucopyranosides does not involve ring opening.

Previous work [1] has shown that the acid-catalysed hydrolysis of most glucopyranosides involves hexose–oxygen bond fission and intermediate carbonium ions. Two mechanisms (A) and (B) are possible.



Mechanism (B) involves ring opening in the rate-determining step; mechanism (A) does not. They might be distinguished in two ways. (1) Mechanism (A) which has been unambiguously demonstrated for several D-glucopyranosyl halides,[2,3] should, by analogy with these cases, give high proportions of products with inverted configuration at position 1. Rapid mutarotation of the products renders this criterion useless for hydrolytic reactions but, given a sufficiently reactive glycoside, it is applicable for other solvents (*e.g.*, methanol). (2) Mechanism (A) should be associated with an oxygen isotope effect since the rate-determining step involves rupture of the hexose–oxygen bond: no effect should be observed for mechanism (B).

Both these criteria have been used. Acid-catalysed solvolyses of a number of phenyl D-glucopyranosides in methanol have been studied and the stereochemical compositions of the products determined. The results support the view, previously put forward by Voss and Wachs [4] who based it on semi-quantitative experiments, that methanolysis, in this system, proceeds largely with inversion of configuration at position 1. The oxygen isotope effect has been investigated for acid-catalysed hydrolysis of methyl α-D-glucopyranoside. The evidence points consistently to mechanism (A).

Experimental

Materials.—Methanol was dried as described by Vogel,[5] and then distilled from anhydrous magnesium perchlorate. Commerical methanesulphonic acid was repeatedly distilled *in vacuo*

* Part III, 1961, 412.

[1] Bunton, Lewis, Llewellyn, and Vernon, *J.*, 1955, 4419.
[2] Rhind-Tutt and Vernon, *J.*, 1960, 4637.
[3] Lemieux and Huber, *Canad. J. Res.*, 1955, **33**, 128.
[4] Voss and Wachs, *Annalen*, 1936, **522**, 240.
[5] Vogel, " Practical Organic Chemistry," Longmans, Green and Co., London, 1948, p. 175.

in an all-glass apparatus. Lithium methanesulphonate was prepared by mixing equivalent solutions, in methanol, of methanesulphonic acid and lithium methoxide; it was recrystallised twice from methanol and dried for 4 hr. at 160°.

Phenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside was prepared from glucose penta-acetate, phenol, and toluene-*p*-sulphonic acid;[6] it had m. p. 127°, $[\alpha]_D^{25}$ −30·7° (*c* 1·0 in benzene). Methylation by the method of McClosky and Coleman[7] gave phenyl 2,3,4,6-tetra-*O*-methyl-β-D-glucopyranoside, m. p. 77°, $[\alpha]_D^{25}$ −46·8° (*c* 1·96 in $CHCl_3$) (Found: C, 62·3; H, 7·3. Calc. for $C_{16}H_{24}O_6$: C, 61·7; H, 7·7%).

Deacetylation of the tetra-*O*-acetate gave phenyl β-D-glucopyranoside, m. p. 173—174·5°, $[\alpha]_D^{25}$ −70·7° (*c* 2·0 in H_2O).

Phenyl α-D-glucopyranoside was made by deacetylation of the tetra-*O*-acetate. After recrystallisation from water and drying *in vacuo*, it had m. p. 169—170°, $[\alpha]_D^{25}$ +181·1° (*c* 0·65 in H_2O).

Methyl α-D-glucopyranoside, recrystallised several times from ethanol, had m. p. 164—165°, $[\alpha]_D^{25}$ +157·8° (*c* 3·0 in H_2O), +163·3° (*c* 2·0 in MeOH).

Methyl β-D-glucopyranoside, made from acetobromoglucose and recrystallised from ethyl acetate, had m. p. 107—108°, $[\alpha]_D^{25}$ −32·6° (*c* 2·7 in H_2O), −33·9° (*c* 2·1 in MeOH).

t-Butyl 2,3,4,6-tetra-O-methyl-β-D-glucopyranoside. t-Butyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (40 g.) was heated in acetone (250 ml.) to 45°. 30% Aqueous sodium hydroxide (250 ml.) was added and then dimethyl sulphate (80 g.) with vigorous stirring, during 1 hr. The methylation procedure was then repeated with half the previous quantities of alkali and dimethyl sulphate. The mixture was boiled for 30 min. and excess of alkali neutralised by carbon dioxide. After evaporation of the solvent, ether-extraction gave 15 g. of a pale yellow oil. This was re-methylated as above. Distillation of the final product gave a pale yellow syrup, b. p. 105°/0·4 mm., n_D^{25} 1·4392, $[\alpha]_D^{15}$ −3·2° (*c* 1·4 in $CHCl_3$) (Found: C, 56·0; H, 9·3. Calc. for $C_{14}H_{28}O_6$: C, 57·5; H, 9·6%). The infrared spectrum showed a strong absorption at 11·25 μ. The poor analytical figures might be taken to mean incomplete methylation; however, the infrared spectrum showed no strong absorption in the region 2·5—2·8 μ.

Other materials were prepared as described previously.[2]

Methanolysis of 2,3,4,6-Tetra-O-methyl-α-D-glucopyranosyl Chloride in the Presence of Methanesulphonic Acid.—The kinetic technique was as previously described.[2] Each run yielded good first-order rate coefficients throughout. Solutions of methanesulphonic acid in anhydrous methanol gave constant titres against standard alkali (in either water or anhydrous methanol as medium) for >24 hr. The products were identified as the isomeric methyl 2,3,4,6-tetra-*O*-methyl-D-glucopyranosides. Analyses were by the infrared technique previously described.[2] Table 1 summarises the results.

TABLE 1. *Methanolysis of 2,3,4,6-tetra-O-methyl-α-D-glucopyranosyl chloride* (~0·1M) *at 25°.*

Electrolyte and concn. (M)		10^3k_1 (min.$^{-1}$)	Proportion of α-glycoside	Electrolyte and concn. (M)		10^3k_1 (min.$^{-1}$)	Proportion of α-glycoside
—	—	3·58	0·06	$LiClO_4$	0·357	5·00	0·06
$Me{\cdot}SO_3H$	0·612	5·50	0·19	LiOAc	0·605	5·55	0·06
,,	1·530	6·52	0·23	LiCl	0·466	6·57	0·31
,,	2·62	7·55	0·24	,,	0·942	7·15	0·35
,,	4·48	9·00	0·24	NaOMe	0·310	6·04	0·06
,,	5·35	10·2	0·24				
$Me{\cdot}SO_3Li$	0·748	4·90	0·19				
,,	0·848	5·20	0·22				

Acid-catalysed Methanolysis of Phenyl D-Glucopyranosides.—Phenol was estimated by means of Folin and Ciocalteu's reagent.[8] Serial aliquot parts (*e.g.*, 0·25 ml.) of a solution, at 25°, of the glucoside (*ca.* 0·05M) in anhydrous methanol containing methanesulphonic acid were run into mixtures of saturated sodium carbonate solution (25 ml.) and water (25 ml.). After addition of the Folin–Ciocalteu reagent (5 ml.), the solutions were shaken for a few minutes, made up to 100 ml. with water, and left for *ca.* 30 min. The colour intensities were then measured on a

[6] Montgomery, Richtmyer, and Hudson, *J. Amer. Chem. Soc.*, 1942, **64**, 690.
[7] McClosky and Coleman, *J. Org. Chem.*, 1945, **10**, 188.
[8] Folin and Ciocalteu, *J. Biol. Chem.*, 1927, **73**, 627.

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Spekker photoelectric absorptiometer fitted with a red filter. Phenol concentrations were calculated by reference to a standard curve. Theoretical and experimental infinity values usually agreed to within 2%. Good first-order rate coefficients (k_1) were found for each run. The following details of an experiment with phenyl α-D-glucopyranoside (0·0395M) and 2·375M-methanesulphonic acid at 25° are illustrative:

Reaction (%)	8·8	15·0	23·8	32·0	44·6	48·7	56·5	66·1
10^3k_1 (min.$^{-1}$)	3·61	3·65	3·60	3·57	3·51	3·41	3·46	3·62

Table 2 shows the results obtained (25°) with three phenyl D-glucopyranosides.

The solutions used for the experiments summarised in Table 2 were also used to follow the changes in optical rotatory power accompanying methanolysis. Portions (10 ml.) of freshly made up solutions were placed in a jacketted polarimeter tube (1 dm.). Constant temperature (25°) was maintained by circulation of water from a thermostat-bath.

TABLE 2. *Methanolysis of phenyl* D-*glucopyranosides* (~0·05M) *at* 25°.

Substrate	[Me·SO_3H] (M)	10^3k_1 (min.$^{-1}$)
Ph α-D-glucopyranoside	2·375	3·55
Ph β-D-glucopyranoside	2·330	1·28
Ph tetra-*O*-methyl-β-D-glucopyranoside ...	2·393	0·41

In each experiment the total amount of the products of methanolysis produced at any time (t) can be calculated from the data in Table 2. By assuming that the corresponding methyl pyranosides are the sole reaction products, the proportion (α) in which the α-isomer is present at a time (t) can be calculated from the rotation of the solution at that time. Table 3 shows the results. The following values of $[\alpha]_D^{25}$ (c ~1·0 in MeOH, [Me·SO_3H] *ca.* 2·0M) were used; +158°, −17°, and +163°, −33·9°, for the α- and β-isomers of methyl 2,3,4,6-tetra-*O*-methyl-D-glucopyranoside and for the α- and β-isomers of methyl D-glucopyranoside, respectively.

TABLE 3. *Products* * *of methanolysis of phenyl* D-*glucopyranosides at* 25°.

(*a*) Ph α-D-glucopyranoside: [Me·SO_3H] = 2·375M; $(\alpha)_{t=0}$ 0·10.

Reaction (%)	16·2	23·3	29·9	35·8	41·3	46·3	50·8	55·0	58·8	62·3	68·4	71·1	99·2
α	0·11	0·10	0·10	0·10	0·11	0·14	0·15	0·17	0·17	0·17	0·18	0·18	0·30

(*b*) Ph β-D-glucopyranoside: [Me·SO_3H] = 2·330M; $(\alpha)_{t=0}$ 0·73.

Reaction (%)	3·1	6·2	9·2	12·0	14·8	17·5	20·1	22·6
α	0·72	0·73	0·73	0·74	0·72	0·73	0·72	0·71
Reaction (%)	25·0	27·4	29·7	31·9	34·0	36·1	38·1	82·4
α	0·72	0·72	0·72	0·73	0·73	0·73	0·73	0·71

(*c*) Ph tetra-*O*-methyl-β-D-glucopyranoside: [Me·SO_3H] = 2·393M; $(\alpha)_{t=0}$ 0·72.

Reaction (%)	9·5	11·3	12·9	15·4	21·7	43·0	45·5	48·1
α	0·72	0·74	0·73	0·74	0·69	0·70	0·70	0·70

* α = Proportion of α-glycoside.

The stabilities of the α- and β-isomers of methyl D-glucopyranoside and 2,3,4,6-tetra-*O*-methyl-D-glucopyranoside, under the conditions of the experiments described above, were determined by following the changes in optical rotation of solutions containing a particular isomer. Approximate initial first-order rate coefficients were calculated by using, in each case, an infinity value corresponding to complete anomerisation. The values obtained for 10^3k_1 (min.$^{-1}$) at 25° with 2·38M-methanesulphonic acid were, respectively, 0·03, 0·04, *ca.* 0·01 and 0·03.

Acid-catalysed Methanolysis of t-Butyl 2,3,4,6-*Tetra*-O-*methyl*-β-D-*glucopyranoside and of* S-*Phenyl* 2,3,4,6-*Tetra*-O-*methyl*-β-D-*thioglucopyranoside*.—Measurements of the optical rotatory power of a solution of t-butyl 2,3,4,6-tetra-*O*-methyl-β-D-glucopyranoside (0·2527 g. in 25 ml.) in methanol containing methanesulphonic acid (1·55M) gave the annexed results (40·5°):

Time (min.)	0	8	17	30	42	58	81	105	121
Rotation	0·075°	0·175°	0·268°	0·378°	0·470°	0·558°	0·675°	0·751°	0·820°
Time (min.)	165	256	357	425	740	1430	3660	4500	
Rotation	0·909°	1·606°	1·170°	1·200°	1·310°	1·467°	2·015°	2·275°	

A sample of the solution taken at 14 hr. from zero was found, after neutralisation, not to reduce Fehling's solution. Isolation of the products gave a mixture of the isomeric methyl

2,3,4,6-tetra-*O*-methyl-D-glucopyranosides, which, by infrared analysis,[2] was shown to contain 46% of the α-isomer.

A plot of optical rotation against time gives a curve with (*a*) an initially steeply rising section followed by (*b*) a linear section of small slope. Extrapolation, to time zero, of (*b*), which may be identified as arising from anomerisation of the products, gives the optical rotation of the products before secondary anomerisation (+1·13°, corresponds to 42% of α-isomer). The value +1·13° can also be used as an infinity for the calculation of first-order rate coefficients, whence $k_1 = 0{\cdot}012$ min.$^{-1}$. The product ratio was unaffected by initial addition of lithium methanesulphonate (1·0M). Methanolysis of t-butyl β-D-glucopyranoside under the same conditions led to a similar product ratio (*ca.* 52% of the α-isomer).

The optical rotation of a solution of *S*-phenyl 2,3,4,6-tetra-*O*-methyl-β-D-thioglucopyranoside (0·1436 g. in 10 ml.) in methanol containing methanesulphonic acid (1·55M) was found to change very slowly at 40·5° with time from −0·630° to −0·585° in 55·6 hr. Darkening prevented further observations. Qualitative comparison with an equivalent solution of phenyl 2,3,4,6-tetra-*O*-methyl-β-D-glucopyranoside showed that the latter compound is at least 100-fold more reactive.

Oxygen Isotope Effect in the Hydrolysis of Methyl α-D-Glucopyranoside.—A solution (1 l.) of methyl α-D-glucopyranoside (200 g.) in aqueous 2·02N-sulphuric acid was prepared. A portion (900 ml.) was kept at 73° ± 1° for 2½ hr. Measurement of the optical rotation showed that 7·5% of the substrate had been hydrolysed. After an excess of sodium hydroxide had been added (cooling), the solution was distilled and the first 300 ml. of distillate were collected. This fraction was refractionated through a spinning-band column (70 cm.) and gave, as middle cut, methanol (1·1 g.), b. p. 64·5°. The remainder of the original solution was kept at 73° until reaction was complete. Methanol was then isolated as described above. The methanol samples were treated with potassium tetrafluorobromate(III) in a fixed reactor.[9] The recovery of oxygen under these conditions was not quantitative. The ratio $^{18}O/^{16}O$ was determined by using an isotope-ratio mass spectrometer. The samples were measured between samples of normal oxygen, obtained from local (Illinois) water by reaction with bromine trifluoride. The results in Table 4, show that methanol taken towards the beginning of the hydrolysis has a significantly lower content of ^{18}O (*ca.* 3%).

TABLE 4. *Oxygen isotope effect in hydrolysis of methyl α-D-glucopyranoside.*

Source of O_2:	Water	$CH_3{\cdot}OH$, 7·5% reaction	Water	$CH_3{\cdot}OH$, 100% reaction	Water
$10^3[^{18}O/^{16}O]$	0·209	0·203	0·210	0·209	0·209

DISCUSSION

Esterification of the solvent, producing water, complicates the study of acid-catalysed reactions in methanol. With glucosides this complication is particularly serious since, in the presence of water, free aldohexoses may be formed and give a variety of secondary products. In the present work this difficulty has been largely avoided by using methanesulphonic acid, which appears to esterify methanol only very slowly, and by the use of relatively low temperatures (25°) and reactive substrates.

We found that the isomeric composition of the products produced by methanolysis of phenyl D-glucopyranosides under our experimental conditions could not be determined by analysis at complete reaction because, first, the rates of anomerisation of the appropriate products were not negligibly slow compared with the overall reaction rates and, secondly, secondary changes arising from esterification of the solvent occurred over the relatively long time required. Consequently, we estimated the ratio in which the isomeric products were formed from each substrate, using results obtained, in each case, during about one half-life. Certain assumptions are necessary: (*a*) that there is no anomerisation of the substrate and (*b*) that the products are methyl D-glucopyranosides and not methyl D-glucofuranosides. Our justification for these is essentially that calculations based on them lead, for each substrate, to values of α (the proportion of product having α-configuration) which

[9] Sheft and Katz, *Analyt. Chem.*, 1957, **29**, 1322.

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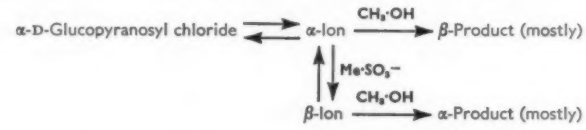
are reasonable and constant over about one half-life (*i.e.*, over times in which the disturbing factors discussed above are not important). Trial calculations showed that if, at any time during the first half-life of a reaction, compounds other than the original substrate and the isomeric methyl D-glucopyranosides had been present, the values of α would not, in general, have been constant and would, in some cases, have been unphysical (*i.e.*, outside the range 0—1·0).

The following particular considerations also support the correctness of our assumptions: (i) With phenyl α-D-glucopyranoside the tendency of α (initially 0·10) to increase after *ca.* 50% reaction is as expected since approximate measurements of the rates of anomerisation of the methyl D-glucopyranosides show that, under our experimental conditions, the proportion of α-isomer present at equilibrium is *ca.* 0·7. Consistently, the values of α (0·72) found for phenyl β-D-glucopyranoside show no such tendency. (ii) With phenyl 2,3,4,6-tetra-*O*-methyl-β-D-glucopyranoside, which cannot form furanoside products, the observed value of α is, within experimental error, the same as that found for the unmethylated compound.

We conclude, therefore, that methanolysis of the three compounds studied, under the specified experimental conditions, gives pyranoside products and proceeds with a high degree of inversion at the position 1 (90% and 72% of inverted product with substrates of α- and β-configuration, respectively).

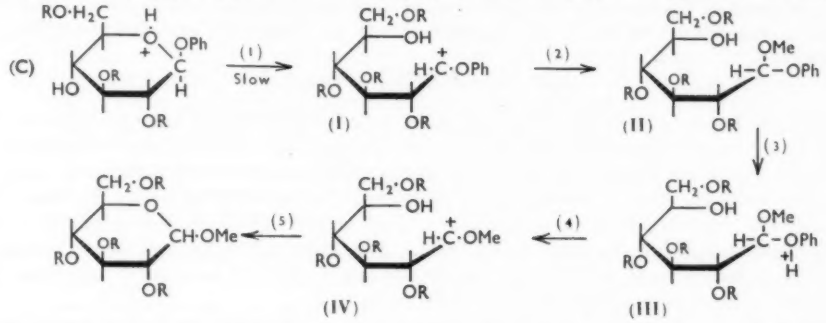
A final complication remains, however, in that these stereochemical results may be partially determined by the high concentrations of methanesulphonate ions necessarily present. To test this possibility the effects of added methanesulphonic acid and of added lithium methanesulphonate on the methanolysis of 2,3,4,6-tetra-*O*-methyl-α-D-glucopyranosyl chloride were studied. This reaction is known [3] to proceed by a carbonium ion process and to give, largely (94%), the product of inverted configuration. It was found (Table 1) that the rate of methanolysis is increased by high concentrations of methanesulphonic acid. This arises, however, from a salt effect and not from the emergence of an acid-catalysed process since lithium methanesulphonate, chloride, acetate, and perchlorate give similar increases in rate. Nevertheless, the methanesulphonate ion has an effect apart



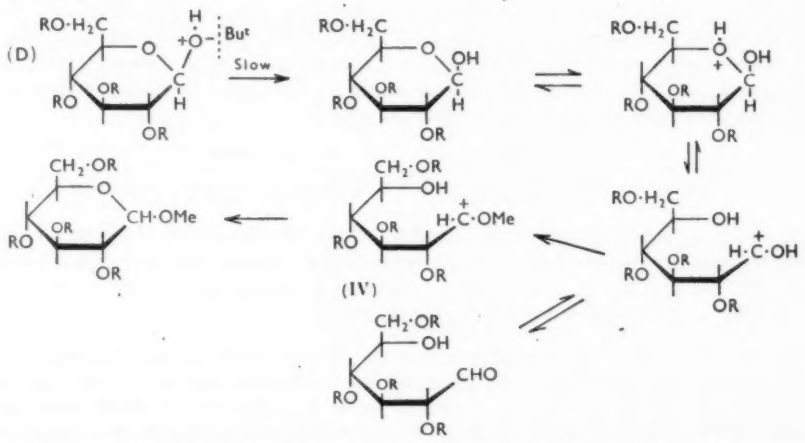
from simply increasing the polar character of the medium since the presence of either the acid or the lithium salt reduces the amount of product of inverted configuration. The same effect is observed with chloride ions, but not with acetate or perchlorate. A possible explanation, previously applied to the effect of chloride ions and discussed in greater detail elsewhere,[2] is provided by the annexed scheme, in which ionisation of the substrate produces an intermediate (ion-pair) without loss of α-configuration (α-Ion). This intermediate either passes directly into products by reaction with methanol or is captured by a methanesulphonate ion to produce a new ion-pair having the β-configuration (β-Ion). Solvolysis of the β-ion leads to a product with the same configuration as the starting material. Hence, the intervention of the methanesulphonate ion reduces the observed overall proportion of product with inverted configuration. However, irrespective of the detailed mechanism of this process, it is clear that any effect on the composition of the products of the acid-catalysed methanolysis of phenyl D-glucopyranosides, specifically due to the presence of the methanesulphonate ion, will be in the direction of reducing the observed proportion of inversion. Hence, the conclusion that these reactions proceed largely with inversion at position 1 is in no way invalidated.

Methanolysis of phenyl D-glucopyranosides proceeding with predominant inversion cannot easily be accommodated by mechanism (B). The scheme (C) shows the steps

which would be involved (R = Me, H). Unless steps **2**—**5** were very rapid, high proportions of inverted product could not arise and, for a given glucoside, the α- and β-isomers should give the same product mixture since the original configurational information contained at the $C_{(1)}$ centre would be lost on passage through the intermediates (I)—(IV). Intermediate (IV) must, in fact, be formed during the methanolysis of t-butyl 2,3,4,6-tetra-*O*-methyl-β-D-glucopyranoside which may be assumed, by analogy with the known



result for hydrolysis, to proceed by alkyl–oxygen bond fission.[10] The scheme (D) shows the steps involved.



Consistently, it was found that the product ratio is quite different from that observed with the corresponding phenyl compound, the isomers being formed in roughly equal amounts (α : β = 42 : 58). Mechanism (B) also fails to account for the relative inertness of *S*-phenyl 2,3,4,6-tetra-*O*-methyl-β-D-thioglucopyranoside to methanolysis. With this compound, even if step **3** were unfavourable, reversal of step **1** should lead, contrary to what was found, to relatively ready anomerisation.

Mechanism (A), on the other hand, is consistent with the observed facts since (*a*) a ring-closed carbonium ion derived from a D-glucopyranose structure would be expected [2,3] to lead to products with a large degree of inversion at position 1 and (*b*) replacement of the glucosidic oxygen atom by sulphur should, since the latter is the less basic, reduce the overall rate of reaction. We conclude, therefore, that methanolysis of phenyl D-glucopyranosides, at least under the specified experimental conditions, proceeds by mechanism (A).

[10] Armour, Bunton, Patai, Selman, and Vernon, *J.*, 1961, 412.

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This conclusion cannot be immediately applied to hydrolytic reactions since, for these, the stereochemical criterion detailed above is inapplicable. However, isotopic analysis of the methanol produced over the first 7% of the hydrolysis of methyl α-D-glucopyranoside showed that the reaction is associated with an appreciable oxygen isotope effect. This can be accommodated by mechanism (A) but not by mechanism (B).

The maximum isotope effect to be expected for the hypothetical process, C–O ⟶ C + O, may be calculated, if complete loss of bonding in the transition state, is assumed, from a simplified version of the equation given by Bigeleisen and Goeppert-Mayer,[11] namely:

$$k_1/k_2 = (m_2^{\ddagger}/m_1^{\ddagger})^{\frac{1}{2}}[1 + G(u)\Delta u]$$

where $u = hc\omega/kT$, Δu is the difference in the value of u for the two isotopic species, and $G(u)$ is a function for which numerical values are available from tables.[11] Taking ω as 1100 cm.$^{-1}$ (*i.e.*, an average for the stretching frequency observed with aliphatic ethers of the type C·O·CH_2 [12]) and calculating $(m_2^{\ddagger}/m_1^{\ddagger})^{\frac{1}{2}}$ from the reduced masses of the fragments obtained by rupture of the hexose–oxygen bond in the conjugate acid of methyl α-D-glucopyranoside,[13] k_1/k_2 is found to be 1·064. The observed value *ca.* 1·03 is, therefore, reasonable for mechanism (A). Mechanism (B) might give rise to a small secondary isotope effect, but the observed effect is too large for this.

The evidence from studies of both methanolysis and hydrolysis of some simple glucopyranosides points, therefore, to the generalisation that acid-catalysed solvolyses of these compounds all proceed by mechanism (A). A possible inconsistency is that, since the acid-catalysed formation of methyl α-D-glucopyranoside from glucose and methanol appears to involve methyl α-D-glucofuranoside as an intermediate, the reverse reaction, *i.e.*, the hydrolysis of methyl α-D-glucopyranoside, must, since it must follow the same path, involve ring-opening. This inconsistency may be removed by assuming that the reaction between glucose and methanol occurs as in the annexed scheme.

If k_1 and k_{-1} are much greater than k_2 and k_{-2} and if the formation of the pyranoside is thermodynamically preferred, then the occurrence of the furanoside as an apparent intermediate in the reaction of glucose and methanol is explained. In the above scheme ring-opening need be assumed only for glucose itself.

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[11] Bigeleisen and Goeppert-Mayer, *J. Chem. Phys.*, 1947, **15**, 261.
[12] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen and Co., Ltd., London, 1957, p. 115.
[13] Bigeleisen and Wolfsberg, " Theoretical and Experimental Aspects of Isotope Effects in Chemical Kinetics," in " Advances in Chemical Physics," Interscience Publ. Inc., New York, 1958, p. 28.

637. *The Transmission of Polar Effects through Aromatic Systems. Part III.* Hammett σ-Constants.*

By R. O. C. Norman, G. K. Radda, and (in part) (Miss) D. A. Brimacombe, P. D. Ralph, and (Miss) E. M. Smith.

The rates of alkaline hydrolysis of ethyl phenylacetate and nine monosubstituted derivatives in aqueous acetone at 25° have been measured. The results support the theory of van Bekkum, Verkade, and Wepster that mesomeric *para*-interaction between substituent and functional centre may affect the σ-value of a substituent. Variations in σ-values arising from the polar effect of the substituent on the resonance interaction of the functional centre with the aromatic nucleus are noted. An improved method of obtaining σ-values is proposed in which use is made only of those reaction series where resonance interaction between the functional centre and the aromatic ring is precluded.

In a recent re-examination of the Hammett equation, van Bekkum, Verkade, and Wepster [1] pointed out that the σ-value attributed to a *para*-substituent depends on the variation in the mesomeric *para*-interaction between the substituent and the functional centre in different reactions. This gives rise to a multiplicity of σ-values which depend on the reactions from which they are derived. One set of values, σ^n, applies when there is no mesomeric *para*-interaction.

To confirm this theory we have examined the rates of alkaline hydrolysis of substituted phenylacetic esters. In these compounds, no resonance interaction can occur between the substituent and the functional centre because of the insulation provided by the intervening methylene group. As a result of these experiments, we have modified the treatment used by van Bekkum, Verkade, and Wepster, on the basis of which a new set of σ-values has been derived.

Table 1. *Rate constants* (l. mole^{-1} sec.$^{-1}$) *for the alkaline hydrolysis of ethyl phenylacetates at* 25°.

Subst. ...	H	*m*-Me	*p*-Me	*p*-OMe	*p*-F	*p*-Cl	*p*-Br	*p*-COMe	*m*-NO_2	*p*-NO_2
10^3k	4·40	3·58	3·18	3·93	6·96	9·71	10·10	13·0	18·4	26·2

Results and Discussion

Second-order rate constants for the alkaline hydrolysis of ethyl phenylacetate and nine monosubstituted ethyl phenylacetates are recorded in Table 1. Using Jaffé's statistical methods,[2] we have obtained the correlation coefficient (r) and the standard deviation (s) for the correlations of our hydrolysis rates with the σ-values compiled by McDaniel and Brown [3] (from the strengths of substituted benzoic acids) and the σ^n-values of van Bekkum, Verkade, and Wepster. The less satisfactory correlation with σ-values ($r = 0{\cdot}957$; $s = 0{\cdot}101$) than with σ^n-values ($r = 0{\cdot}983$; $s = 0{\cdot}063$) arises principally because of the deviations of the points for *p*-halogen and *p*-methoxyl. For example, the rates of hydrolysis indicate that the *p*-Me group is more strongly electron-releasing than *p*-OMe. This is consistent with the σ^n-values of the groups (−0·129 and −0·111 respectively [1]) but not with the σ-values [3] (−0·170 and −0·268), the more negative σ-value of *p*-OMe arising from its conjugation with the carboxyl group in *p*-anisic acid. Thus our results are in agreement with the theory of van Bekkum, Verkade, and Wepster.[1]

However, the annexed plot of log (k/k_0) against σ^n-values, for our hydrolyses, reveals that the points for our three substituents of greatest electron-attracting power (*m*-NO_2,

* Part II, *J.*, 1961, 2938.

[1] van Bekkum, Verkade, and Wepster, *Rec. Trav. chim.*, 1959, **78**, 815.
[2] Jaffé, *Chem. Rev.*, 1953, **53**, 191.
[3] McDaniel and Brown, *J. Org. Chem.*, 1958, **23**, 420.

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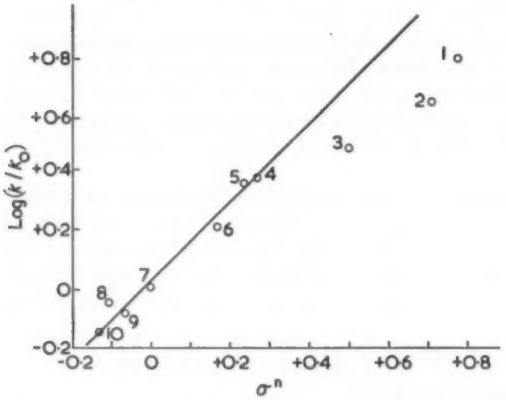
p-NO_2, and *p*-COMe) lie considerably below the best straight line for the other seven compounds. These deviations are not due to entropy effects since the pre-exponential factors for the hydrolysis of ethyl phenylacetate and its *m*- and *p*-nitro-derivatives are constant (Table 2) (cf. Leffler [4]).

Our results give good correlation with those from the alkaline hydrolysis of substituted benzyl acetates,[5] from the alkaline hydrolysis of ethyl phenylacetates in aqueous ethanol,[6] and from the *N*-chlorination of *N*-benzylacetamides.[7] These reaction series are similar to ours in that mesomeric *para*-interaction is prevented by the methylene group. Further, as with our results, the points for the *m*- and *p*-NO_2 substituents are abnormal, the deviations being in the same direction as in ours.* These similarities suggest a weakness in the method by which the σ^n-values for the *m*-NO_2, *p*-NO_2, and *p*-COMe groups were derived.

van Bekkum, Verkade, and Wepster assumed that the σ^n-values of *meta*-substituents, and of *p*-NO_2 and *p*-COMe substituents (derived from reactions in which no resonance



Plot of log (k/k_0) *against* σ^n*-values of substituents in ethyl phenylacetate.*

1, *p*-NO_2. 2, *m*-NO_2. 3, *p*-COMe. 4, *p*-Br. 5, *p*-Cl. 6, *p*-F. 7, H. 8, *p*-OMe. 9, *m*-Me. 10, *p*-Me.

interaction occurs between these groups and the functional centre), are the same as their well-established σ-values.[1] But this assumption neglects one other type of interaction: namely, the polar effect of the substituent on the resonance interaction of the functional centre with the aromatic nucleus. Two of the reactions used by these workers for deriving the σ^n-values of *p*-NO_2 and *p*-COMe groups were the ionisations of the *para*-substituted benzoic acids and the *para*-substituted phenylacetic acids. Now, in the equilibrium of

TABLE 2. *The pre-exponential factor.*

Subst.	H	*m*-NO_2	*p*-NO_2	Subst.	H	*m*-NO_2	*p*-NO_2
10^3k (25°) ...	4·40	18·5	26·2	10^3k (55°) ...	23·6	86·5	124
10^3k (40°) ...	10·4	42·0	59·1	$\log_{10} PZ$	6·6	6·7	6·6

benzoic acid with its anion, there is evidence that the conjugation of the carboxyl group with the benzene ring, represented by the contribution of structure (I) to the molecule, is responsible for stabilising the acid by about 1 kcal. $mole^{-1}$ more than the corresponding conjugation in the benzoate ion, represented by the contribution of structure (II).[8]

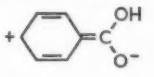
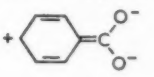
* The *p*-COMe substituent was not studied in any of these reactions, nor was the *m*-NO_2 substituent studied by Watkinson and his collaborators.[6]

[4] Leffler, *J. Org. Chem.*, 1955, **20**, 1202.
[5] Tommila and Hinshelwood, *J.*, 1938, 1801; Tommila, *Ann. Acad. Sci. Fennicae*, 1942, **59**, *A*, No. 4.
[6] J. G. Watkinson, personal communication.
[7] Williams, *J.*, 1930, 37.
[8] Taft in "Steric Effects in Organic Chemistry," ed. M. S. Newman, John Wiley and Sons, Inc., New York, 1956, p. 581.

A polar *para*-substituent in benzoic acid will affect the contribution of forms (I) and (II) to their respective hybrids. For example, an electron-attracting group will decrease their contributions and thereby reduce the difference in their importance, corresponding to an acid-strengthening effect, but this cannot occur in *para*-substituted phenylacetic acids, where there is no interaction between the carboxyl group and the aromatic ring. Therefore, we expect that the σ-values of *p*-NO_2 and *p*-COMe groups calculated from the strengths of the benzoic acids will be larger than those calculated from the strengths of the phenylacetic acids or from reactions on other systems with insulating methylene groups. This is confirmed by our results. The same argument applies in principle to *meta*-substituents, though presumably to a smaller extent, for the effect of the substituent on the resonance interactions represented by forms (I) and (II) has to be relayed through a carbon atom. Possibly this is why it is only for the strongly electron-attracting nitro-group that a deviation is observed for a *meta*-substituent.

The corollary to this argument is that the resonance interaction of a group of $+M$ type with the benzene ring should be enhanced by an electron-attracting substituent. Evidence for this has been adduced by Wepster [9] from measurements of the basic strengths of substituted dimethylanilines.

According to these arguments, the σ-value of a *para*-substituent derived from a reaction series in which the functional centre is conjugated with the aromatic ring, should differ from its σ^n-value because of the effect of this substituent on the conjugation. It may also differ because of direct conjugation between functional centre and substituent. van Bekkum, Verkade, and Wepster have taken account only of the latter effect in their

(I)   (II)

treatment; we wish to emphasise that the former may make a significant difference to the σ-values derived from a particular reaction series.

We propose a new scale of σ-values, based on reaction series in which the functional centre is insulated from the benzene ring. We have examined the rather small number of reactions which satisfy this criterion for the derivation of new σ-values and have chosen only those for which data referring to five or more substituents are available and which have ρ-values greater than 0·5. σ-Values have been derived only for substituents which have been studied in at least three of the reactions.

The hydrolyses reported in this paper were initially chosen as the basis for the new σ-values, this reaction being assigned the value $\rho = 1$. ρ-Values for five reaction series and σ-values for nine substituents were then obtained, by using the method employed by

TABLE 3. *Values of* σ^n *and* σ_G.

Subst.	*p*-Me	*m*-Me	*p*-OMe	*p*-F	*p*-Cl	*p*-Br	*m*-Cl	*m*-NO_2	*p*-NO_2
σ^n	−0·129	−0·069	−0·111	+0·168	0·238	0·265	0·373	0·710	0·778
σ_G	−0·129	−0·105	−0·097	+0·143	0·256	0·281	0·334	0·576	0·708

Jaffé in compiling Hammett σ-constants.[2] A plot of these σ-values against σ^n-values was linear except for the points for the *m*- and *p*-NO_2 groups. This probably indicates that it is only strongly polar groups which significantly affect the conjugation of a second substituent with the aromatic nucleus. The slope of the regression line obtained by including all values except for the *m*- and *p*-NO_2 groups was used to relate our new σ-constants to the σ^n-scale, and the revised values are set out in Table 3. The new σ has been designated σ_G because, since it is a polarisation parameter which refers to the *ground-state* electron distribution, it has the same basis as the σ_G-constant derived from a recent treatment of electrophilic aromatic substitution.[10]

[9] Wepster, *Rec. Trav. chim.*, 1956, **75**, 1473.
[10] Knowles, Norman, and Radda, *J.*, 1960, 4885.

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TABLE 4. *Reactions from which* σ_G *and* ρ *were obtained.*

Reaction	Solvent	Temp.	ρ	s	r	n	Ref.
$Ar{\cdot}CH_2{\cdot}CO_2Et + OH^-$	60% Me_2CO	25°	1·069	0·029	0·996	8	
$Ar{\cdot}CH_2{\cdot}CO_2Et + OH^-$	85·4% EtOH	24·8	1·168	0·021	0·998	5	6
$Ar{\cdot}CH_2{\cdot}CO_2H$ (pK_a)	H_2O	25	0·612	0·027	0·989	8	11
$Ar{\cdot}CH_2{\cdot}OAc + OH^-$	56% Me_2CO	25	0·894	0·019	0·998	8	5
$Ar{\cdot}CH_2{\cdot}NHAc + Cl_2$	40% AcOH	18	−1·256	0·049	0·987	5	7

The reactions from which σ_G-values were obtained are shown in Table 4 together with the corresponding reaction constant, ρ, the standard deviation, s, the correlation coefficient, r, and the number, n, of substituents used in the derivation.

EXPERIMENTAL

Materials.—Substituted phenylacetic acids were prepared, where necessary, by methods reported in the literature and were converted into their ethyl esters by the Fischer–Speier method. Liquid esters were purified by fractional distillation, and solid esters by repeated recrystallisations from light petroleum (b. p. of various ranges). The physical data and references to the preparation of these compounds are shown in Table 5. M. p.s are recorded for two of the esters which were previously reported as liquids.

We thank Dr. J. G. Watkinson of Manchester University for ethyl *p*-methyl-, *p*-chloro-, and *p*-bromo-phenylacetate.

Solvent.—" AnalaR " acetone was dried (K_2CO_3) and fractionally distilled. It was diluted with freshly boiled, distilled water to give a mixture containing 60% (v/v) of acetone. Rate measurements carried out with " AnalaR " acetone which had not been purified in this way gave identical results.

TABLE 5. *Phenylacetic acids and their ethyl esters.*

	Acid		Ethyl ester			
Subst.	M. p.	Ref.	M. p.	Ref.	B. p.°/mm.	Ref.
H					227/758	12
m-Me	62°	13			122—123/18	14
m-NO_2	118—120	15	11·5—12·5°	*a*	127—135/0·25	16
p-Me	94	13			134—135/25	17
p-OMe	85—86	18			143—144/11	19
p-F	84·5	20	34	*b*	128—130/31	21
p-Cl			33—33·5	22		
p-Br			31—31·5	23		
p-COMe			62—63	24		
p-NO_2			63	25		

[a,b] M. p.s not previously reported. [a] Found: C, 57·1; H, 5·2; N, 7·2. Calc. for $C_{10}H_{11}NO_4$: C, 57·4; H, 5·3; N, 6·7%. [b] Found: C, 66·1; H, 6·3. Calc. for $C_{10}H_{11}FO_2$: C, 66·0; H, 6·1%.

Rate Measurements.—The procedure followed was essentially that described previously by Tommila and Hinshelwood.[5] Atmospheric carbon dioxide was excluded from standard alkali solutions with Carbosorb guard tubes, and these solutions were restandardised frequently. Initial concentrations of alkali and ester were equal (*ca.* 0·01M), and the extent of hydrolysis

[11] Dippy and Williams, *J.*, 1934, 161 and 1888; Baker, Dippy, and Page, *J.*, 1937, 1774; Dippy and Page, *J.*, 1938, 357.
[12] Perkin, *J.*, 1896, **69**, 1175.
[13] Radziszewski and Wispek, *Ber.*, 1885, **18**, 1280.
[14] Senkowski, *Monatsh.*, 1888, **9**, 855.
[15] de Boer and Backer, *Rec. Trav. chim.*, 1954, **73**, 229.
[16] Muenzen, Cerecedo, and Sherwin, *J. Biol. Chem.*, 1926, **68**, 504.
[17] Claus and Kroseberg, *Ber.*, 1887, **20**, 2051.
[18] King and McMillan, *J. Amer. Chem. Soc.*, 1946, **68**, 2335.
[19] Cain, Simonsen, and Smith, *J.*, 1913, **103**, 1036.
[20] Dippy and Williams, *J.*, 1934, 1466.
[21] Corse, Jones, Soper, Whitehead, and Behrens, *J. Amer. Chem. Soc.*, 1948, **70**, 2837.
[22] Mehner, *J. prakt. Chem.*, 1900, **62**, 565.
[23] Wislicenus and Grützner, *Ber.*, 1909, **42**, 1933.
[24] Papa, Schwenk, and Klinsberg, *J. Amer. Chem. Soc.*, 1946, **68**, 2133.
[25] Maxwell, *Ber.*, 1879, **12**, 1767.

was studied from approximately 10 to 80% of completion. Each reaction obeyed second-order kinetics. The results recorded in Table 1 are the averages of at least two runs in each case, rate coefficients from different runs agreeing to within ±2%.

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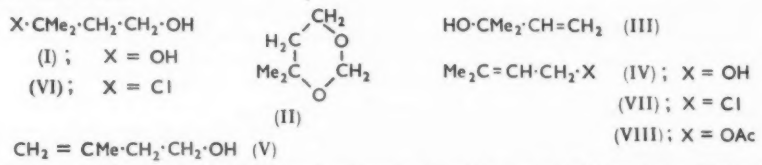
638. *Studies in the Synthesis of Terpenes. Part VI.* Some Reactions of 3-Methylbutane-1,3-diol.*

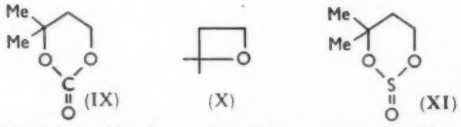
By T. G. HALSALL and A. R. HANDS.

Some reactions of 3-methylbutane-1,3-diol are described.

SYNTHESIS of a monoterpene usually involves the use of a C_5 intermediate. Apart from isoprene the C_5 compound potentially most readily and cheaply available on an industrial scale is 3-methylbutane-1,3-diol (I). This can be prepared by hydrolysis of the product (II) of the Prins reaction between formaldehyde and isobutene.[1] Recently we have studied the reactions of the diol (I) and its conversion into the three alcohols (III), (IV), and (V), and the corresponding chlorides. Some of the new compounds obtained in this work are described.



Treatment of the diol (I) with dry hydrogen chloride gave 3-chloro-3-methylbutan-1-ol (VI). Distillation over phosphoric oxide of the crude product gave 1-chloro-3-methylbut-2-ene (VII) which was converted into 3-methyl-2-enyl acetate (VIII) when heated with sodium acetate in acetic acid. Hydrolysis of this acetate gave the corresponding alcohol (IV). Dehydrochlorination of the chloro-alcohol (VI) with *NN*-diethylaniline gave the homoallylic alcohol (V), the pyrophosphate of which is the biogenetic precursor of the terpenes.[2-4]



Me2CCl·CH2·CH2·O·SO·Cl (XII)

The diol (I) readily formed a cyclic carbonate (IX). The band of the infrared spectrum due to its carbonyl group occurred at quite different frequences in carbon tetrachloride (1772 cm.$^{-1}$) and chloroform (1735 cm.$^{-1}$). Pyrolysis of the carbonate gave 3-methylbut-3-en-1-ol (V) (38%) and 2-methylbut-3-en-2-ol (III) (19%). This reaction is, however, not of great preparative value because very careful fractionation is necessary to separate the mixture of alcohols obtained. The formation of the alcohols, rather than of 2,2-dimethyloxetan (X), is in line with the result of Searles, Hummel, Nukina, and Throckmorton[5]

* Part V, *J.*, 1960, 4931.

[1] Rosen and Arundale, U.S.P. 2,368,494.
[2] Chaykin, Law, Phillips, Tchen, and Bloch, *Proc. Nat. Acad. Sci. U.S.A.*, 1958, **44**, 998.
[3] Eggerer, Lynen, Henning, and Kessel, *Angew. Chem.*, 1958, **70**, 738.
[4] Eggerer and Lynen, *Annalen*, 1960, **630**, 59.
[5] Searles, Hummel, Nukina, and Throckmorton, *J. Amer. Chem. Soc.*, 1960, **82**, 2928.

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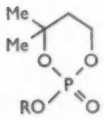
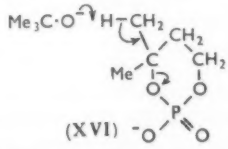
who have shown that if hydrogen is present on the β-carbon of a 1,3-diol its cyclic carbonate is catalytically decomposed by base to an unsaturated alcohol rather than to an oxetan. The corresponding cyclic sulphite (XI) was obtained when the diol (I), thionyl chloride, and pyridine, in a 1 : 1 : 2-molar ratio, were kept in dry benzene. From the chloro-alcohol (VI) the chlorosulphite (XII) was formed.

In view of the current interest [2,3] in the rôle of C_5 phosphates in the biogenesis of terpenes some phosphates were prepared from the diol (I). Treatment of it (1 mol.) with phenyl phosphorodichloridate (1 mol.) and pyridine (2 mol.) in benzene afforded the cyclic phosphate (XIII). With diphenyl phosphorochloridate, 3-hydroxy-3-methylbutyl diphenyl phosphate (XIV) was obtained. Hydrolysis of the cyclic phenyl phosphate with sodium hydroxide solution gave the cyclic hydrogen phosphate (XV) (42%) and



(XIII); R = Ph
(XV); R = H

$HO{\cdot}CMe_2{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}PO(OPh)_2$
(XIV)



(XVI)

phenyl dihydrogen phosphate (13%), isolated as cyclohexylamine salt. More than one of the P–O bonds of the cyclic phosphate can therefore be split. It was considered possible that treatment of the cyclic phosphate (XV) with sodium t-butoxide would lead to abstraction of a proton from one of the methyl groups followed by fission of the $C_{(3)}$–O bond (cf. XVI) with the formation of the monophosphate of the methylbutenol (V). However, no elimination product was isolated and only the cyclic acid was recovered.

Experimental

M. p.s were determined on a Kofler block and are corrected.

1-Chloro-3-methylbut-2-ene.—3-Methylbutane-1,3-diol (70 g.) was saturated with dry hydrogen chloride (increase in wt., 39 g.). The mixture was distilled under reduced pressure, the fraction (93 g.) of b. p. 20—120°/14 mm. being collected. The upper layer of this distillate was separated and dried ($MgSO_4$; P_2O_5). Redistillation from phosphorus pentoxide (19 g.) gave 1-chloro-3-methylbut-2-ene (37 g., 53%), b. p. 30—40°/14 mm., $n_D^{19.5}$ 1·4490 (lit.: n_D^{20} 1·4480,[6] 1·4485 [7]); $\nu_{max.}$ 838 cm.$^{-1}$ (CH=C), no bands at 890 (=CH_2) or 990 (CH=CH_2) cm.$^{-1}$.

The nitrosochloride formed plates (from carbon disulphide), m. p. 133°, which sublimed at 150° (bath temp.)/15 mm. to give pale blue prisms, m. p. 80—90° immediately after sublimation. After one week at 20° the sublimate was almost colourless and had m. p. 118—119° (lit.,[8] 117°).

The *isothiouronium picrate* formed yellow needles (from ethanol), m. p. 179—180° (decomp.) (Found: C, 38·6; H, 4·3; N, 18·9; S, 8·6. $C_{12}H_{15}N_5O_7S$ requires C, 38·6; H, 4·1; N, 18·7; S, 8·6%).

In a further experiment, 3-methylbutane-1,3-diol (50 g.) was saturated with dry hydrogen chloride at 0° (increase in weight, 29 g.). The excess of hydrogen chloride was removed at 20°/15 mm. The mixture was then dissolved in ether (600 c.c.) and shaken with an excess of sodium carbonate until effervescence ceased. The solution was filtered and dried ($MgSO_4$), and the ether then removed by distillation. Distillation of the residue gave a fraction (13·0 g.; 22%), b. p. 50—65°/15 mm., $n_D^{17.5}$ 1·4490 (Found: C, 48·6; H, 9·0; Cl, 28·5. $C_5H_{11}ClO$ requires C, 49·0; H, 9·0; Cl, 28·9%), which from the analytical data must be essentially *3-chloro-3-methylbutan-1-ol* although the boiling point range is not small. The fraction gave *3-chloro-3-methylbutyl 1-naphthylurethane* as plates (from light petroleum, b. p. 40—60°), m. p. 84° (Found: C, 66·0; H, 6·3; Cl, 12·1; N, 4·7. $C_{16}H_{18}ClNO_2$ requires C, 65·9; H, 6·2; Cl, 12·1; N, 4·8%). A further fraction (30·6 g.; 52%) had b. p. 65—72°/15 mm., $n_D^{17.5}$ 1·4483 (Found: Cl, 25·1%).

3-Chloro-3-methylbutyl Acetate.—3-Chloro-3-methylbutan-1-ol (50 g.) and acetic anhydride (200 c.c.) were heated under reflux for 3 hr. After it had cooled, the mixture was added to

[6] Nazarov and Azerbaev, *J. Gen. Chem.* (*U.S.S.R.*), 1948, **18**, 414.
[7] Ultee, *Rec. Trav. chim.*, 1949, **68**, 125.
[8] Jones and Chorley, *J.*, 1946, 832.

ice (800 g.) and stirred vigorously for 2 hr. An excess of potassium carbonate was added and the mixture was extracted with ether (2 × 200 c.c.), and the product fractionally distilled under reduced pressure to give 3-*chloro*-3-*methylbutyl acetate* (5·9 g., 9%), b. p. 47—51°/14 mm., n_D^{18} 1·4350 (Found: C, 50·8; H, 8·5; Cl, 21·7. $C_7H_{13}ClO_2$ requires C, 51·1; H, 8·0; Cl, 21·6%).

Conversion of 1-*Chloro*-3-*methylbut*-2-*one into* 3-*Methylbut*-2-*enyl Acetate*.—1-Chloro-3-methylbut-2-ene (12·5 g.), anhydrous sodium acetate (20·2 g.), and acetic acid (100 c.c.) were stirred and heated at 60—70° for 2 hr. The cooled product was poured into water (250 c.c.) and an excess of potassium carbonate was added. Ethereal extraction afforded a product which was distilled under reduced pressure to give 3-methylbut-2-enyl acetate (12·5 g., 81%), b. p. 40—44°/15 mm., n_D^{17} 1·4304, $\nu_{max.}$ 824w cm.$^{-1}$ (Found: C, 65·65; H, 9·6. Calc. for $C_7H_{12}O_2$: C, 65·5; H, 9·45%) (lit.:[9] b. p. 74°/55 mm., n_D^{20} 1·4298).

The acetate was hydrolysed to 3-methylbut-2-en-1-ol, b. p. 45—52°/15 mm., n_D^{24} 1·4400; $\nu_{max.}$ 834m cm.$^{-1}$ (–C=CH–) (lit.: n_D^{19} 1·4439). The 1-*naphthylurethane* crystallised from light petroleum as long needles, m. p. 104° (Found: C, 74·95; H, 6·7; N, 5·7. $C_{16}H_{17}NO_2$ requires C, 75·3; H, 6·7; N, 5·5%).

3-*Methylbut*-3-*en*-1-*ol*.—A mixture of 3-chloro-3-methylbutan-1-ol (50 g.) and *NN*-diethylaniline (250 c.c.) was distilled, the fraction boiling between 70° and 180° being collected. The upper layer of the distillate was separated, dried, and fractionally distilled to give 3-methylbut-3-en-1-ol (23 g., 65%), b. p. 129—133°, n_D^{15} 1·4371; $\nu_{max.}$ (liq. film), 1650s (C=C), and 886s (C=CH_2) cm.$^{-1}$ (lit.:[10] b. p. 130°, n_D^{16} 1·4354).

The 1-*naphthylurethane* crystallised from light petroleum as needles, m. p. 66° (Found: C, 75·3; H, 6·6; N, 5·2. $C_{16}H_{17}NO_2$ requires C, 75·3; H, 6·7; N, 5·5%).

4,4-*Dimethyl*-1,3-*dioxan*-2-*one*.—3-Methylbutane-1,3-diol (50 g.), diethyl carbonate (60 g.), and sodium (0·3 g.) were heated at 130° (bath temp.) for 2 hr. The temperature was then raised to 170° during 1 hr. The mixture was cooled, and the resulting solid was filtered off and recrystallised from ethanol to give 4,4-*dimethyl*-1,3-*dioxan*-2-*one* (47 g., 76%) as prisms, m. p. 78—79°; $\nu_{max.}$ (CCl_4), 1772s ($CHCl_3$), 1735s, (Nujol) 1725s cm.$^{-1}$ [Found: C, 55·2; H, 7·9%; *M* (micro-Rast), 116. $C_6H_{10}O_3$ requires C, 55·4; H, 7·85%; *M*, 130].

Pyrolysis of 4,4-*Dimethyl*-1,3-*dioxan*-3-*one*.—4,4-Dimethyl-1,3-dioxan-2-one (50 g.) was placed in a 150 c.c. distilling flask which was then immersed in Wood's metal previously heated to 300—320°. The material (29·5 g.; n_D^{19} 1·4385) distilling at 180—200° was collected, starting material (5·3 g.) remaining in the flask. The distillate was redistilled through a 12-cm. fractionating column packed with stainless steel gauze to give 2-methylbut-3-en-2-ol (6·2 g., 19%), b. p. 98—108°, n_D^{18} 1·4180; $\nu_{max.}$ 990s, 918s cm.$^{-1}$ (CH=CH_2) (lit.:[11] b. p. 96—98°/744 mm., n_D^{20} 1·4168), and 3-methylbut-3-en-1-ol (12·6 g., 38%), b. p. 130—135°, n_D^{18} 1·4365; $\nu_{max.}$ 886s cm.$^{-1}$ (C=CH_2) (lit.:[10] b. p. 130°, n_D^{16} 1·4384). A further fraction (7%), b. p. 139—145°, was collected. 4,4-Dimethyl-1,3-dioxan-2-one (6·9 g., 14%) remained in the distilling flask.

4,4-*Dimethyl*-1,3,2-*dioxathian*-2-*one*.—3-Methylbutane-1,3-diol (10·4 g.) was dissolved in dry benzene (200 c.c.), and dry pyridine (15·8 g.) was added. Thionyl chloride (11·9 g.) in benzene (50 c.c.) was added dropwise during 1 hr., the mixture being stirred and cooled in ice. It was kept at 20° for ½ hr. and then filtered, and the filtrate evaporated at 35°/13 mm. The residue was distilled to give 4,4-*dimethyl*-1,3,2-*dioxathian*-2-*one* (10 g., 67%), b. p. 79—80°/13 mm., n_D^{14} 1·4545 (Found: C, 39·95; H, 6·75; S, 21·3. $C_5H_{10}O_3S$ requires C, 40·0; H, 6·7; S, 21·35%).

3-*Chloro*-3-*methylbutyl Chlorosulphite*.—3-Chloro-3-methylbutan-1-ol (12 g.) was dropped during ½ hr. into thionyl chloride (70 g.), and the mixture was then heated under reflux for 2½ hr. The thionyl chloride was distilled off at atmospheric pressure and the residue was distilled twice to give 3-*chloro*-3-*methylbutyl chlorosulphite* (12·8 g., 64%), b. p. 108—110°/15 mm., n_D^{15} 1·4845 (Found: C, 29·6; H, 5·0; Cl, 34·3; S, 15·3. $C_5H_{10}Cl_2O_2S$ requires C, 29·3; H, 4·9; Cl, 34·6; S, 15·6%).

1,1-*Dimethyltrimethylene Phenyl Phosphate*.—3-Methylbutane-1,3-diol (14·4 g.) was dissolved in benzene (100 c.c.)–pyridine (21·4 g.), and phenyl phosphorodichloridate (29·3 g.) was added. The mixture was kept at 20° for 24 hr. and then filtered. The filtrate was evaporated to give 1,1-*dimethyltrimethylene phenyl phosphate* (33·5 g., 100%) as an oil, n_D^{26} 1·5113, which solidified, m. p. 64—72°, after 4 days (Found: C, 54·4; H, 6·25. $C_{11}H_{15}O_4P$ requires C, 54·55; H, 6·25%);

[9] Young and Webb, *J. Amer. Chem. Soc.*, 1951, **73**, 780.
[10] Laforgue, *Compt. rend.*, 1948, **227**, 352.
[11] Campbell and Eby, *J. Amer. Chem. Soc.*, 1941, **63**, 2683.

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$\nu_{max.}$ 1294s cm.$^{-1}$ (P=O) (Jones and Katritzky [12] give 1290 cm.$^{-1}$ from ν(P=O) in ethyl trimethylene phosphate).

3-Hydroxy-3-methylbutyl Diphenyl Phosphate.—3-Methylbutane-1,3-diol (10·4 g.) in benzene (20 c.c.)–pyridine (7·9 g.) was kept at 20° for 24 hr. with diphenyl phosphochloridate (26·85 g.). The mixture was filtered and the filtrate evaporated to give *3-hydroxy-3-methylbutyl diphenyl phosphate* (33·5 g., 100%) as an oil, n_D^{20} 1·5280 (Found: C, 60·4; H, 6·6. $C_{17}H_{21}O_5P$ requires C, 60·7; H, 6·3%).

1,1-Dimethyltrimethylene Hydrogen Phosphate.—1,1-Dimethyltrimethylene phenyl phosphate (67 g.) was heated at 100° for 30 min. with 27% aqueous sodium hydroxide (150 c.c.). The mixture was cooled and acidified with concentrated hydrochloric acid, and ether (250 c.c.) was added. After the mixture had been cooled it was filtered and the separated solid was extracted with ether in a Soxhlet apparatus. On cooling of the extract, *1,1-dimethyltrimethylene hydrogen phosphate* crystallised as short needles (19·5 g., 42%), m. p. 63—68° (decomp.) (Found: C, 36·1; H, 6·7; active H, 0·6. $C_5H_{11}O_4P$ requires C, 36·15; H, 6·7; active H, 0·6%). The *cyclohexylamine salt* formed needles, m. p. 198—199° (from ethanol) (Found: C, 49·3; H, 8·5. $C_{11}H_{24}NO_4P$ requires C, 49·8; H, 9·1%).

The filtrate described above was separated, and the ether layer was evaporated to give a residue which was taken up in ethyl acetate. Addition of cyclohexylamine gave *di(cyclohexylammonium) phenyl phosphate* as needles (8·8 g.), m. p. 214° (from ethanol) (Found: C, 57·85; H, 9·1; N, 7·2. $C_{18}H_{33}N_2O_4P$ requires C, 58·1; H, 8·95; N, 7·55%). Treatment of the salt with 2N-hydrochloric acid, followed by extraction with ether, afforded phenyl dihydrogen phosphate, m. p. 97—98° (sealed tube).

Action of Sodium t-Butoxide on 1,1-Dimethyltrimethylene Hydrogen Phosphate.—The acid ester (3·32 g., 0·02 mole) was added to a solution of sodium (0·92 g., 0·04 g.-atom) in t-butyl alcohol (125 c.c.), and the mixture was heated under reflux for 24 hr. Acidification of the cooled mixture with concentrated hydrochloric acid (3·56 c.c., 0·04 mole) and evaporation to dryness at 60°/16 mm. gave a solid. Extraction of this with ether (Soxhlet) afforded only unchanged material (0·1 g., 3%), m. p. 76—78°.

The authors thank Professor E. R. H. Jones for his interest, and Dr. F. R. Atherton and Dr. K. R. Farrer for helpful comments on phosphorylation. One of them (A. R. H.) thanks Messrs. A. Boake Roberts and Co., Ltd. for a bursary. This firm also kindly provided the 3-methylene-1,3-diol.

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[*Received, February 20th,* 1961.]

[12] Jones and Katritzky, *J.*, 1960, 4376.

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639. *Purines, Pyrimidines, and Glyoxalines. Part XV.*[1] *Acetyluracils from Amines and Amino-acids. A New Method for the Study of N-Terminal Residues in Proteins.*

By J. H. DEWAR and G. SHAW.

α-Acetyl-β-ethoxy-*N*-ethoxycarbonylacrylamide reacts with amines and amino-acids, forming acid-stable 5-acetyluracils. The reaction has been applied to the determination of the *N*-terminal residues in insulin and ribonuclease.

PART IV [2] of this series described the preparation of 5-cyanouracils by reaction of amines, amino-acids, and glycylglycine with the ethoxyacrylamide derivative (II). Development of this reaction for use in *N*-terminal assay studies of peptides and proteins was limited by the lability of the 5-cyano-group in the uracils to acid-hydrolysis, which may give rise

[1] Part XIV, Shaw and Butler, *J.*, 1959, 4040.
[2] Atkinson, Shaw, and Warrener, *J.*, 1956, 4118.

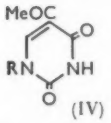
under different conditions to mixtures of the corresponding carboxyamide, carboxylic acid, and decarboxylated material.

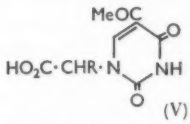
We now report the preparation of analogous 5-acetyluracils which are completely immune to hydrolysis by strong acid and may be used to advantage in *N*-terminal studies of proteins.

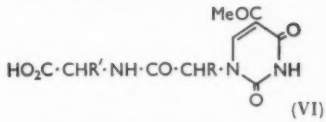
N-Acetoacetylurethane (from diketen and urethane; cf. Part XII [3]) with ethyl orthoformate and acetic anhydride readily gave a good yield of the crystalline ethoxyacrylamide (I; R = Et). This with ammonia or methylamine gave the 5-acetyluracils (IV; R = H or Me), and with aniline gave the linear anilinoacrylamide (III; R = Ph) which cyclised to the acetyluracil (IV; R = Ph) when heated at its melting point or warmed with aqueous alkali. Hydrolysis of the ethoxyacrylamide (I; R = Et) under mild conditions with sodium hydroxide also gave the hydroxyacrylamide (I; R = H).

(I) Me·CO·C(:CH·OR)·CO·NH·CO_2Et CN·C(:CH·OEt)·CO·NH·CO_2Et (II)

Me·CO·C(:CH·NHR)·CO·NH·CO_2Et (III)


(IV)


(V)


(VI)

Similar reaction of the ethoxyacrylamide (I; R = Et) with most of the L-amino-acids normally found in proteins, in dilute sodium hydroxide solution or, in some cases, in aqueous triethylamine, for short periods, gave corresponding 5-acetyl-1-uracilacetic acids (V) in substantially quantitative yields and, except for the derivatives from L-cysteine and L-tryptophan, as crystalline solids. The acetyluracils are useful derivatives of amino-acids and may be separated, identified, and estimated by paper chromatography, ion-exchange, ultraviolet absorption spectrophotometry, and by reactions of the exocyclic ketone group, *e.g.*, with 2,4-dinitrophenylhydrazine. L-Aspartic and L-glutamic acid were exceptional in forming linear derivatives (III) in sodium hydroxide solution, but the corresponding uracils were readily prepared by acid hydrolysis of the easily cyclised L-asparagine and L-glutamine derivatives. Other linear derivatives were also obtained from the urethane (I; R = Et) and L-cysteine, L-arginine, and L-proline in sodium hydrogen carbonate solution or aqueous triethylamine when the reaction was not prolonged. Further treatment of the linear derivative from arginine with warm sodium hydrogen carbonate solution gave the cyclic product. The linear acrylamide from L-cysteine with dilute sodium hydroxide rapidly gave the cyclic product, and with sodium hydroxide and iodine it gave the uracil derived from L-cystine. The last compound was also prepared in the normal manner from the ethoxyacrylamide (I; R = Et) and L-cystine. In all these reactions there appears to be no combination of the ethoxyacrylamide (I; R = Et) with any of the other functional groups present in the amino-acids, *e.g.*, alcoholic or phenolic hydroxyl, thiol, the NH group in histidine, or the guanidine group of arginine.

Acetyluracil derivatives (VI) of several dipeptides have also been prepared as readily crystallising solids from the ethoxyacrylamide (I; R = Et) in aqueous triethylamine or sodium hydroxide without rupture of the peptide bond. In these reactions cyclisation appears to occur even more readily than with the amino-acids, and linear acrylamides were not isolated. Acid hydrolysis of the peptide derivatives gave the uracil derived from the *N*-terminal amino-acid, together with a free amino-acid, as the sole products and these were readily characterised by paper chromatography.

To establish the stability of the pyrimidine ring to acid hydrolysis under conditions comparable to those required for protein hydrolysis, samples of acetyluracil-1-acetic acids

[3] Ralph, Shaw, and Naylor, *J.*, 1959, 1169.

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(V) derived from glycine, L-leucine, L-aspartic acid, and L-histidine were boiled with 6N-hydrochloric acid for 7 hr. Ultraviolet absorption spectra of the hydrolysates indicated a quantitative recovery of the uracils.

The reactions have also been applied to the determination of the *N*-terminal residues in insulin and ribonuclease. Reactions of the proteins with the ethoxyacrylamide (I; R = Et) were carried out in aqueous triethylamine for 1 hr. at room temperature. The resulting solid derivatives were hydrolysed and the evaporated solutions extracted with ethyl acetate. Paper chromatograms showed in the case of insulin two absorbing spots only, which corresponded exactly with the uracils derived from glycine and L-phenylalanine; and from ribonuclease a single spot corresponding to the bisuracil derivative of L-lysine was the sole absorbing material. Also chromatograms of the aqueous-hydrolysis solutions showed a single absorbing spot which corresponded to the ε-monouracil derivative of L-lysine. The spots were further characterised as from ketones by spraying them with a solution of 2,4-dinitrophenylhydrazine. In these reactions removal of the excess of ethoxyacrylamide (I; R = Et) appears to be unnecessary since it is completely hydrolysed by acid to simple volatile products.

Experimental

Paper chromatography (ascending) was carried out on Whatman No. 1 paper at room temperature with the following solvents (ratios in volume proportions): (1) butan-1-ol–acetic acid–water (4 : 1 : 5), (2) propan-2-ol–ammonia (*d* 0·88)–water (7 : 1 : 3), (3) butan-1-ol saturated with water, (4) propan-2-ol–10N-hydrochloric acid–water (17 : 5 : 3). The acetyluracils were detected on paper as dark absorbing spots under an ultraviolet lamp (Hanovia Chromatolight) or as yellow spots by spraying them with a solution of 2,4-dinitrophenylhydrazine hydrochloride in water or methanol. Spectral measurements were made on an Optica double-beam recording CF4 spectrophotometer.

α-Acetyl-β-ethoxy-N-ethoxycarbonylacrylamide.—A mixture of *N*-acetoacetylurethane [3] (70 g.), ethyl orthoformate (61 g.), and acetic anhydride (101 ml.) was boiled under reflux for 1 hr. The red solution was evaporated *in vacuo* to an oil which rapidly crystallised. The solid was washed with ether which removed most of the colour. The *acrylamide* (58 g.) recrystallised from light petroleum (b. p. 60—80°) containing a little benzene as needles, m. p. 90° (Found: C, 51·9; H, 6·3; N, 6·4. $C_{10}H_{15}NO_5$ requires C, 52·2; H, 6·6; N, 6·1%). This compound is referred to below as the " ethoxyacrylamide."

α-Acetyl-β-hydroxy-N-ethoxycarbonylacrylamide.—The ethoxyacrylamide (1 g.) was shaken for a few minutes with 2N-sodium hydroxide (3 ml.), a clear solution being obtained. This was cooled and acidified to precipitate the *hydroxyacrylamide* (0·2 g.), which separated from a little water as needles, m. p. 57—58° (Found: C, 47·75; H, 5·35; N, 6·3. $C_8H_{11}NO_5$ requires C, 47·7; H, 5·5; N, 6·95%), giving a red colour with ferric chloride solution.

5-Acetyluracil.—The ethoxyacrylamide (2 g.) was warmed with 3N-ammonia (50 ml.) until a clear solution was obtained. This was evaporated to remove the excess of ammonia, cooled, and acidified with acetic acid, to give after a short time a crystalline precipitate. *5-Acetyluracil* (1·2 g.) separated from ethanol (*ca.* 250 ml.) as prisms, m. p. 283—285° (decomp.). Bergmann and Johnson [4] give m. p. 294° (decomp.) (Found: C, 46·8; H, 3·65; N, 18·0. Calc. for $C_6H_6N_2O_3$: C, 46·75; H, 3·95; N, 18·2%). The 2,4-*dinitrophenylhydrazone* crystallised from acetic acid as orange-red needles, m. p. 276° (decomp.) (Found: C, 43·3; H, 3·2; N, 24·7. $C_{12}H_{10}N_6O_6$ requires C, 43·15; H, 3·0; N, 25·15%).

5-Acetyl-1-methyluracil.—A suspension of the ethoxyacrylamide (0·3 g.) in water was warmed for a few minutes with a little aqueous methylamine: a clear solution was rapidly obtained. This was cooled, and acidified with acetic acid to precipitate *5-acetyl-1-methyluracil* (0·22 g.) which recrystallised from ethanol as plates, m. p. 234° (Found: C, 50·05; H, 4·85; N, 16·95. $C_7H_8N_2O_3$ requires C, 50·0; H, 4·8; N, 16·7%).

5-Acetyl-1-phenyluracil.—A solution of the ethoxyacrylamide (1·15 g.) and aniline (0·5 ml.) in ethanol (5 ml.) was warmed for 30 min., then set aside overnight whereupon crystals separated. *α-Acetyl-β-anilino-N-ethoxycarbonylacrylamide* (0·96 g.) separated from ethanol as

[4] Bergmann and Johnson, *Ber.*, 1933, **66**, 1492.

prisms, m. p. 118° (Found: C, 60·7; H, 5·75; N, 10·4. $C_{14}H_{16}N_2O_4$ requires C, 60·85; H, 5·85; N, 10·15%). This linear derivative (0·5 g.) was heated at 170° (bath), effervescing and then solidifying. The residue, *5-acetyl-1-phenyluracil* (0·41 g.), crystallised from ethanol as needles, m. p. 269° (decomp.) (Found: C, 62·3; H, 4·2; N, 12·4. $C_{12}H_{10}N_2O_3$ requires C, 62·6; H, 4·4; N, 12·2%). The same compound was also obtained by warming the linear acrylamide with sodium hydroxide solution until a clear solution was obtained. Acidification of this then precipitated the phenyluracil.

Aminoacrylamides from α-Amino-acids and the Ethoxyacrylamide.—(a) *L-Cysteine.* A solution of L-cysteine hydrochloride (1·95 g.) in water (5 ml.) and triethylamine (4·3 ml.) was warmed with the ethoxyacrylamide (2·76 g.) for 3 min. The cooled solution was acidified with 10N-hydrochloric acid to precipitate a gum which rapidly crystallised. The *acrylamide* (2·5 g.) recrystallised from ethyl acetate–ether as needles, m. p. 146° (Found: C, 43·05; H, 5·2; N, 8·75. $C_{11}H_{16}N_2O_6S$ requires C, 43·45; H, 5·3; N, 9·2%). The compound gave an intense purple colour with sodium nitroprusside in alkaline solution.

(b) *L-Aspartic acid.* A solution of L-aspartic acid (1·12 g.) in 2N-sodium hydroxide (7·5 ml.) and water (2·5 ml.) was warmed with the ethoxyacrylamide (1·84 g.) for 10 min. The cooled solution was acidified with 10N-hydrochloric acid (2·5 ml.) to give after a short time a crystalline precipitate. The *acrylamide* (2·5 g.) separated from water as needles, m. p. 200° (decomp.) (Found: C, 45·55; H, 5·15; N, 8·8. $C_{13}H_{16}N_2O_8$ requires C, 45·6; H, 5·1; N, 8·85%). The same compound was obtained when the reaction was carried out in aqueous triethylamine or sodium hydrogen carbonate solution.

(c) *L-Glutamic acid.* L-Glutamic acid (1·84 g.) in 2N-sodium hydroxide (7·5 ml.) was warmed with the ethoxyacrylamide (1·84 g.) for 10 min. The cooled solution was acidified with hydrochloric acid and continuously extracted with ether for 3 hr. The extract was evaporated and the dried residue crystallised from acetone–light petroleum (b. p. 40—60°), to give the *acrylamide* (3 g.) as needles, m. p. 158° (Found: C, 47·35; H, 5·6; N, 8·8. $C_{13}H_{18}N_2O_8$ requires C, 47·3; H, 5·5; N, 8·5%). The same compound may be similarly prepared in aqueous triethylamine or sodium hydrogen carbonate solution.

(d) *L-Proline.* A mixture of L-proline (0·24 g.), water (1 ml.), triethylamine (0·8 ml.), and the ethoxyacrylamide (0·46 g.) was warmed for 15 min. on a water-bath. The cooled solution was acidified with 10N-hydrochloric acid (0·6 ml.) to give a solid precipitate. The *acrylamide* (0·6 g.) crystallised from a small quantity of water as needles, m. p. 75° (Found: C, 48·4; H, 6·6; N, 8·8. $C_{13}H_{18}N_2O_6,1\frac{1}{2}H_2O$ requires C, 48·0; H, 6·6; N, 8·6%).

(e) *L-Arginine.* A mixture of L-arginine (0·72 g.) in water (10 ml.) containing sodium hydrogen carbonate (0·5 g.) and the ethoxyacrylamide (0·92 g.) in ethanol (10 ml.) was shaken at room temperature for 4 hr., a clear solution being obtained. This was evaporated to a small volume and acidified with 10N-hydrochloric acid (1 ml.): a gel separated. A portion of this, when boiled with water and then cooled, gave a crystalline precipitate. The gel soon crystallised when seeded with the crystalline sample. The *acrylamide hydrochloride hydrate* (1·5 g.) recrystallised from water as needles, m. p. 145° (Found: C, 41·1; H, 6·35; N, 17·7. $C_{14}H_{23}N_5O_6,HCl,H_2O$ requires C, 40·8; H, 6·35; N, 17·0%).

Cyclisation of α-Acetyl-β-carboxymethylaminoacrylamides.—Cysteine and cystine. The linear acrylamide from L-cysteine (0·915 g.) was warmed for 10 min. with 2N-sodium hydroxide (3·6 ml.) in an atmosphere of hydrogen. The cooled solution was acidified with 10N-hydrochloric acid to precipitate a little gum. The mixture was diluted with water and continuously extracted with ether. Evaporation of the extract gave a semi-solid residue from which the *acetyluracil* (0·5 g.) was obtained as an amorphous solid by precipitation of an acetone solution with light petroleum (b. p. 40—60°). It gave an intense purple colour with an alkaline solution of sodium nitroprusside. The compound also gave only one absorbing spot on paper chromatograms. The foregoing acrylamide from L-cysteine (0·59 g.) in N-sodium hydroxide (6·9 ml.) was treated with a solution of iodine (4·95 ml. of a 5·6% solution in 20% potassium iodide). After a few minutes the solution was covered with ethyl acetate and acidified with 10N-hydrochloric acid. The solution was extracted once more with ethyl acetate. Evaporation of the combined extracts gave the crystalline *acetyluracil* derivative of L-cystine (0·5 g.) which gave no colour with sodium nitroprusside in alkaline solution. The same compound was detected on paper chromatograms from the reaction of the ethoxyacrylamide with L-cystine in dilute sodium hydroxide solution. M. p.s, analyses, and other physical data are recorded in Table 1.

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5-Acetyluracil-1-acetic Acids from α-Amino-acids and the Ethoxyacrylamide.—M. p.s, analyses, and other data are recorded in Table 1. (a) *Glycine.* The ethoxyacrylamide (0·5 g.) was warmed for 5 min. with a solution of glycine (0·18 g.) in 2N-sodium hydroxide (2·5 ml.). The cooled solution was acidified with 10N-hydrochloric acid (0·5 ml.) to precipitate the *uracil* (0·5 g.).

(b) L-*Arginine.* A mixture of L-arginine (0·72 g.) in water (10 ml.) containing sodium hydrogen carbonate (0·5 g.), and the ethoxyacrylamide (0·92 g.) in ethanol (10 ml.) was set aside at 40—50° over a week-end. The cooled solution was acidified with hydrochloric acid and extracted with ether. The aqueous phase was evaporated to dryness *in vacuo*, and the

TABLE 1. *5-Acetyl-1-uracilacetic acids* (V).

No.	R	Generating acid [a, g]	M. p.[b]	R_F of ketone in solvent			R_F of 2,4-dinitrophenylhydrazone in solvent		
				1	2	3	1	2	3
1	H [c]	Glycine	200°	0·48	0·59	0·04	0·73	0·70	0·24
2	Me [c]	Alanine	174	0·66	0·66	0·07	0·82	0·78	0·28
3	Pr^i [c]	Valine	196	0·84	0·77	0·21	0·89	0·86	0·42
4	Bu^i [d]	Leucine	153	0·85	0·80	0·31	0·90	0·92	0·47
5	Bu^s [d]	Isoleucine	187	0·87	0·82	0·27	0·90	0·91	0·45
6	Ph·CH$_2$ [c]	Phenylalanine	214	0·83	0·79	0·25	0·89	0·88	0·41
7	*p*-HO·C$_6$H$_4$·CH$_2$ [e]	Tyrosine	183	0·78	0·71	0·17	0·86	0·83	0·34
8	HO·CH$_2$ [e, j]	Serine	216	0·51	0·64	0·04	0·72	0·76	0·20
9	HS·CH$_2$ [f, p]	Cysteine	143	0·65	0·55	0·08	0·74	0·68	0·30
10	C$_9$H$_8$N$_2$O$_6$S·S·CH$_2$ [d]	Cystine	197	0·52	0·56	0·01	0·89	0·70	0·04
11	Me·CH(OH) [h, j]	Threonine	96	0·63	0·70	0·08	0·81	0·80	0·30
12	MeS·CH$_2$·CH$_2$ [f]	Methionine	159	0·79	0·79	0·16	0·88	0·83	0·34
13	C$_8$H$_6$N·CH$_2$ [m]	Tryptophan	166	0·82	0·74	0·20	0·89	0·79	0·37
14	HO$_2$C·CH$_2$ [f, j, k]	Aspartic acid	209	0·58	0·57	0·01	0·75	0·68	0·09
15	H$_2$N·CO·CH$_2$ [e]	Asparagine	157	0·51	0·66	0·04	0·65	0·70	0·13
16	HO$_2$C·CH$_2$·CH$_2$ [h, j, l]	Glutamic acid	180	0·62	0·63	0·01	0·79	0·71	0·03
17	H$_2$N·CO·CH$_2$·CH$_2$ [e]	Glutamine	187	0·39	0·65	0·03	0·68	0·74	0·14
18	H$_2$N·C(:NH)·NH·[CH$_2$]$_3$ [c]	Arginine	>300	0·51	0·74	0·06	0·74	0·76	0·25
19	C$_6$H$_5$N$_2$O$_2$·[CH$_2$]$_4$ [c, o]	Lysine	152	0·62	0·70	0·06	0·75	0·73	0·20
20	C$_3$H$_3$N$_2$·CH$_2$ [i, m]	Histidine	236	0·25	0·69	0·06	0·51	0·73	0·23

No.	Found (%) C	H	N	Formula	Required (%) C	H	N
1	41·55	4·5	12·75	$C_8H_8N_2O_6,H_2O$	41·75	4·4	12·2
2	41·65	5·6	11·15	$C_9H_{10}N_2O_5,1\frac{1}{2}H_2O$	41·95	5·3	10·9
3	51·65	5·7	10·8	$C_{11}H_{14}N_2O_5$	51·95	5·55	11·0
4	51·2	6·0	10·05	$C_{12}H_{18}N_2O_6,\frac{3}{4}H_2O$	51·15	6·25	9·95
5	53·75	5·95	10·4	$C_{12}H_{16}N_2O_5$	53·7	6·0	10·45
6	60·05	4·6	9·15	$C_{15}H_{14}N_2O_5$	59·6	4·65	9·25
7	53·1	4·9	8·15	$C_{15}H_{14}N_2O_6,H_2O$	53·55	4·8	8·35
8	42·35	4·3	10·9	$C_9H_{10}N_2O_6,\frac{3}{4}H_2O$	42·25	4·55	10·95
9	42·8	5·0	10·4	$C_9H_{10}N_2O_5S,\frac{1}{2}C_3H_6O$	42·95	4·25	10·3
10	39·65	3·45	10·55	$C_{18}H_{18}N_4O_{10}S_2,1\frac{1}{2}H_2O$	39·95	3·9	10·35
11	44·05	5·4	10·3	$C_{10}H_{12}N_2O_6,H_2O$	43·8	5·15	10·2
12	46·0	4·8	9·35	$C_{11}H_{14}N_2O_5S$	46·15	4·95	9·8
13	57·7	5·6	11·9	$C_{17}H_{18}N_3O_5,\frac{3}{4}H_2O$	57·55	4·7	11·85
14	44·35	3·7	10·4	$C_{10}H_{10}N_2O_7$	44·45	3·75	10·35
15	42·4	4·65	14·9	$C_{10}H_{11}N_3O_6,H_2O$	41·85	4·55	14·65
16	43·75	4·6	9·45	$C_{11}H_{12}N_2O_7,H_2O$	43·7	4·65	9·25
17	45·15	4·95	14·1	$C_{11}H_{13}N_3O_6,\frac{1}{2}H_2O$	45·2	4·85	14·4
18	40·35	5·6	19·0	$C_{12}H_{17}N_5O_6,HCl,\frac{1}{2}H_2O$	40·4	5·35	19·65
19	46·6	5·25	12·45	$C_{18}H_{30}N_4O_8,2\frac{1}{2}H_2O$	46·45	5·4	12·05
20	41·6	4·55	16·5	$C_{12}H_{13}N_4O_5,HCl,H_2O$	41·55	4·35	16·15

[a] The amino-acids all have the L-configuration. [b] With decomp. [c] Needles from water. [d] Prisms from water. [e] Plates from water. [f] Needles from ethyl acetate–light petroleum (b. p. 40—60°). [g] Needles from acetone. [h] Needles from ethyl acetate. [i] Needles from ethanol. [j] Isolated from the aqueous solution by continuous extraction with ether. [k] Prepared by boiling the asparagine derivative with 6N-hydrochloric acid for 2 hr. [l] Prepared by boiling the glutamine derivative with 6N-hydrochloric acid for 2 hr. [m] The hydrochloride crystallised from the aqueous solution after evaporation to a small volume. [n] Amorphous solid from acetone–ether. [o] The bis-uracil derivative. [p] The compound retained a little acetone. [q] Compounds were dried over phosphoric oxide at room temperature and 0·5 mm. before analysis.

residue extracted with dimethylformamide. The extract was added to ether to produce a solid precipitate of the *uracil hydrochloride hemihydrate* (1 g.) which was purified by repeating the last process.

Other 5-acetyluracil-1-acetic acids prepared in yields of 75—100% as under (a) above are described in Table 1. The uracils derived from L-alanine, L-serine, and L-tyrosine were also similarly prepared in aqueous triethylamine. Compounds which did not separate from the acidified reaction mixture were isolated by continuous extraction with ether.

Preparation of 2,4-Dinitrophenylhydrazones of 5-Acetyluracil-1-acetic Acids.—Small quantities of the derivatives were prepared for paper chromatography from each of the acetyluracils derived from amino-acids, by addition of a solution of 2,4-dinitrophenylhydrazine in 2N-hydrochloric acid or methanolic sulphuric acid to solutions of the uracils in hot water or methanol. The derivatives were centrifuged off and recrystallised, generally from water, ethanol, or aqueous ethanol, and finally collected by centrifugation. The products were not analysed. R_F values are recorded in Table 1.

5-Acetyluracils from Peptides and the Ethoxyacrylamide.—M. p.s, analyses, and other data are recorded in Table 2. (a) *Glycyl-L-tyrosine.* A solution of the peptide (0·25 g.) in N-sodium

TABLE 2. *5-Acetyluracil peptides* (VI).

					R_F in solvent		
No.	R	R′	Generating acid	M. p.[c]	1	2	3
1	H	H[a]	Glycylglycine	271°	0·48	0·63	0·02
2	H	Me[a]	Glycyl-DL-alanine	258	0·84	0·85	0·04
3	H	Bu^i[a]	Glycyl-DL-leucine	237	0·82	0·78	0·15
4	H	Ph·CH_2[a]	Glycyl-DL-phenylalanine	251	0·79	0·77	0·12
5	H	*p*-HO·C_6H_4·CH_2[a]	Glycyl-L-tyrosine	239	0·70	0·68	0·06
6	H	C_8H_6N·CH_2[b]	Glycyl-L-tryptophane	275	0·77	0·72	0·09
7	Bu^i	H[a]	DL-Leucylglycine	240	0·83	0·83	0·16

	Found (%)				Required (%)		
No.	C	H	N	Formula	C	H	N
1	45·05	4·25	15·5	$C_{10}H_{11}N_3O_6$	44·6	4·1	15·6
2	45·0	4·3	14·65	$C_{11}H_{13}N_3O_6,\frac{1}{2}H_2O$	45·2	4·85	14·4
3	51·35	5·85	12·7	$C_{14}H_{19}N_3O_6$	51·7	5·9	12·9
4	56·0	4·6	11·65	$C_{17}H_{17}N_3O_6$	56·8	4·75	11·7
5	52·1	4·5	11·25	$C_{17}H_{17}N_3O_7,H_2O$	51·9	4·85	10·7
6	54·95	4·7	13·75	$C_{19}H_{18}N_4O_6,H_2O$	54·8	4·85	13·45
7	49·9	5·9	12·6	$C_{14}H_{19}N_3O_6,\frac{1}{2}H_2O$	50·3	6·05	12·6

[a] Needles from water. [b] Needles from ethanol. [c] With decomp.

hydroxide (2·5 ml.) was warmed with the ethoxyacrylamide (0·23 g.) for a few minutes. The cooled solution was acidified with hydrochloric acid to precipitate the uracil (0·31 g.). (b) *Glycyl-L-tryptophan.* The peptide (0·07 g.) in water (1 ml.) and triethylamine (0·2 ml.) was warmed for a few minutes with the ethoxyacrylamide (0·07 g.). The cooled solution was acidified with hydrochloric acid to precipitate a gum which rapidly crystallised to give the *uracil* (0·1 g.). Other peptide derivatives prepared in the same way in yields of 80—100% are recorded in Table 2.

Hydrolysis of Peptide Derivatives.—The acetyluracil derived from glycyl-L-tyrosine (2—3 mg.) was heated at 100° with 6N-hydrochloric acid for 7 hr. The solution was evaporated to dryness, and the residue chromatographed on paper. A single absorbing spot was observed with R_F values 0·6 (solvent 2) and 0·84 (solvent 4) corresponding to the acetyluracil derived from glycine, R_F 0·6 (solvent 2) and 0·84 (solvent 4), which was run as a control. Also when the paper chromatograms from the hydrolysate were sprayed with dinitrogen tetroxide and ammonia, or with diazotised sulphanilic acid and sodium hydroxide solution, a coloured spot (R_F 0·65 in solvent 2 and 0·63 in solvent 4) was observed which corresponded with L-tyrosine (R_F 0·65 in solvent 2 and 0·64 in solvent 4). Hydrolysis of other peptide derivatives gave analogous results.

Stability of 5-Acetyluracil-1-acetic Acids to Acid Hydrolysis.—Stock solutions of the acetyluracil-1-acetic acids derived from glycine, L-leucine, L-histidine, and L-aspartic acid containing 20 mg. in 100 ml. of 6N-hydrochloric acid were prepared. Portions of each of these were diluted to a concentration of 1 mg. per 100 ml. of 0·5N-hydrochloric acid, and the absorption spectra of

these solutions were measured. Portions of the stock solutions were boiled under reflux for 7 hr., then diluted to the same concentration as the standards, and the absorption spectra were measured. The results, recorded in Table 3, indicated quantitative retention of the uracil structure in all cases.

TABLE 3. *Stability of 5-acetyluracil-1-acetic acids* (V) *to acid hydrolysis.*

		Absorption spectra			
		Before hydrolysis		After hydrolysis	Recovery [a]
R	Generating acid	$\lambda_{max.}$ (mμ)	ε	$\lambda_{max.}$ (mμ)	(%)
H	Glycine	229	11,350	228	101
		283	14,500	283	
Bu^{i}	L-Leucine	230	9,300	230	102
		286	12,650	286	
$C_3H_3N_2{\cdot}CH_2$	L-Histidine	223	12,650	223	100
		284	14,300	284	
$HO_2C{\cdot}CH_2$	L-Aspartic acid	230	9,100	230	99·5
		282	12,600	282	

[a] An average of the yields calculated from measurements of the extinction coefficients at both maxima.

Determination of the N-Terminal Residues in Insulin and Ribonuclease.—(a) *Insulin.* A solution of insulin (0·09 g.) in water (1 ml.) and triethylamine (0·05 ml.) with the ethoxyacrylamide (0·025 g.) was set aside at room temperature with occasional shaking for 1 hr. The solution was then acidified with hydrochloric acid to give a solid precipitate. This was centrifuged off and washed successively with small amounts of water, acetone, and ether, and collected by centrifugation. The derivative (0·02 g.) was boiled under reflux with 6N-hydrochloric acid (4 ml.) for 7 hr. The solution was evaporated to dryness, and the residue dissolved in water and extracted with ethyl acetate. The extract was evaporated and the residue chromatographed on paper. Two absorbing spots only were observed with R_F values in solvent 1 0·45 and 0·83, and in solvent 2 0·58 and 0·75 which corresponded with the acetyluracils derived from glycine (R_F 0·45 in solvent 1 and 0·58 in solvent 2), and L-phenylalanine (R_F 0·83 in solvent 1 and 0·75 in solvent 2).

(b) *Ribonuclease.* A solution of ribonuclease (0·05 g.) in water (1 ml.) and triethylamine (0·05 ml.) with the ethoxyacrylamide (0·025 g.) was set aside at room temperature with occasional shaking for 1 hr. The solution was acidified to give a solid precipitate which was centrifuged off and washed with water, acetone, and ether. The dried material weighed 0·05 g. The derivative (0·05 g.) was boiled under reflux with 6N-hydrochloric acid (5 ml.) for 7 hr., then evaporated to dryness. The residue was dissolved in water and the solution extracted with ethyl acetate. Chromatography of the extract on paper showed one absorbing spot (R_F 0·59 and 0·7 in solvents 1 and 2 respectively) which corresponded to the bisacetyluracil derivative of L-lysine (R_F 0·59 and 0·7 in solvents 1 and 2). The aqueous solution from the hydrolysis was also chromatographed on paper; a single absorbing spot (R_F 0·34 in solvent 1) was observed which corresponded to the ε-monouracil derivative of L-lysine (R_F 0·34 in solvent 1). A solution of the last-mentioned uracil admixed with the bisuracil was obtained as follows. A solution of L-lysine monohydrochloride (1·8 g.) in water (5 ml.) was treated with cupric carbonate (2 g.). After 5 min., 2N-sodium hydroxide (5 ml.) was added, giving a deep blue solution. This was filtered, then treated with portions of 2N-sodium hydroxide (total 12 ml.) and the ethoxyacrylamide (total 2·3 g.) alternately during 30 min. with ice-cooling. The solution was set aside overnight at 0°, filtered from a small amount of precipitate, and acidified with 10N-hydrochloric acid (5 ml.). The solution was again filtered, boiled, and treated with hydrogen sulphide. The cupric sulphide was removed, and the solution evaporated to a gum. A portion of this was chromatographed on paper; two absorbing spots were observed (R_F 0·58 and 0·34 in solvent 1); the first of these corresponded to the bisuracil from L-lysine (R_F 0·59), and the second to the ε-monouracil derivative. The formation of the latter material from ribonuclease confirms the structure.

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640. *Steroids and Walden Inversion. Part XLVIII.* The Solvolysis of Some 3-Epimeric 4,4-Dimethyl-steroid Toluene-p-sulphonates.*

By C. W. Shoppee and G. A. R. Johnston.

Solvolysis of the 3-epimeric 4,4,14α-trimethyl-5α-cholest-8-en-3-yl and 4,4-dimethyl-5α-cholestan-3-yl toluene-*p*-sulphonates gives the expected rearranged tertiary alcohols and hydrocarbons, accompanied in each case by the unrearranged alcohol (or acetate) with retained configuration. No unrearranged alcohol (or acetate) with inverted configuration was found.

The solvolyses proceed by unimolecular heterolysis, at rates only slightly greater than that, under comparable conditions, of cyclohexyl toluene-*p*-sulphonate, so that synartetic acceleration is absent.

The structural and kinetic features of the solvolyses are discussed, and a mechanism to accommodate them is suggested.

The occurrence of nucleophilic molecular rearrangement in saturated systems requires fulfilment of two conditions: (1) an initial bond fission to give an electron-deficient centre, and (2) a decrease in free energy. In rigid cyclohexane systems, the rate and the product(s) of rearrangement depend also on the geometry of the original system. Thus solvolysis of isobornyl chloride (Cl equatorial) to yield products of the camphene series is faster by a factor of 10^5 than that of bornyl chloride (Cl axial) to give the same products,[1,2] whilst the acid-catalysed dehydration with acetic anhydride of *exo*-methylnopinol (OH equatorial) furnishes isobornyl acetate, whereas *endo*-methylnopinol (OH axial) affords α-fenchyl acetate.[3]

Solvolytic reactions of suitable steroid derivatives do not normally lead to ring contraction: † $^+CHR{-}CH_2R \longrightarrow CHR_2{-}CH_2^+$, because the free-energy change is in the wrong direction. Only 1β- and 12β-substituted steroids, where the substituent is equatorial and adjacent to a bridgehead, can comply with the thermodynamic condition (2): $^+CHR{-}CMeR_2 \longrightarrow CHR_2{-}{}^+CMeR$; in 4α-, 6α-, 7β-, and 11α-substituted steroids, although the substituent is equatorial and adjacent to a bridgehead, the thermodynamic situation is one of approximate balance: $^+CHR{-}CHR_2 \rightleftharpoons R_2CH{-}{}^+CHR$. Accordingly, alcoholysis of the 12β-toluene-*p*-sulphonate or 12β-methanesulphonate of rockogenin (3β,12β-dihydroxy-5α,20α,22β,25β-isospirostane) yields a C-nor-D-homo-steroid,[6] and we expect to realise the transformation of an appropriate steroid 1β-alcohol into an A-nor-B-homo-steroid.

4,4-Dimethyl-5α-steroids can fulfil the thermodynamic condition (2), and appropriate 3β-substituted derivatives should undergo solvolysis to give A-nor-steroids, whilst the epimeric 3α-substituted derivatives should undergo solvolysis, without contraction of ring A but with migration of the 4β-methyl group. We have observed such changes in solvolyses of the 3-epimeric 4,4,14α-trimethyl-5α-cholest-8-en-3-yl (lanost-8-en-3-yl) and 4,4-dimethyl-5α-cholestan-3-yl toluene-*p*-sulphonates.

4,4,14α-Trimethyl-5α-cholest-8-en-3β-yl toluene-*p*-sulphonate (as I) in refluxing aqueous acetone in the presence of sodium acetate gave the 3β-alcohol (as II; R = H) (5%) (unaccompanied by the epimeric 3α-alcohol), the tertiary A-nor-alcohol (as III; R = H) (22%), and the derived A-nor-5α-cholest-8-ene (as IV) (72%) (which appeared to be

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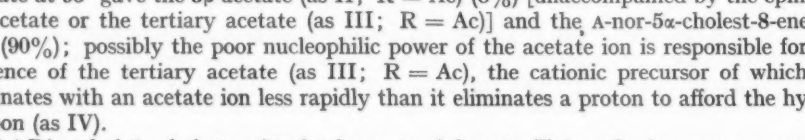
† The Favorski reaction applied to 5α- and 5β-cholestan-3-one leads to A-nor-5α- and A-nor-5β-cholestane derivatives,[4] but is considered to involve fission of an intermediate cyclopropanone.[5]

[1] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons Ltd., London, 1953, p. 515.
[2] Shoppee, *Chem. and Ind.*, 1952, 86.
[3] Burrows and Eastman, *J. Amer. Chem. Soc.*, 1959, **81**, 245.
[4] Evans, Paulet, Shoppee, and Winternitz, *J.*, 1957, 1451.
[5] Loftfield, *J. Amer. Chem. Soc.*, 1950, **72**, 632; 1951, **73**, 4707.
[6] Hirschmann, Snoddy, Hiskey, and Wendler, *J. Amer. Chem. Soc.*, 1954, **76**, 4013; cf. Wendler, Hirschmann, Slates, and Walker, *ibid.*, 1955, **77**, 1632.

homogeneous and free from the isopropenyl and endocyclic isomerides); dehydration of the tertiary A-nor-alcohol with phosphoryl chloride and pyridine gave the same hydrocarbon. Heating the same ester with acetic acid in the presence or absence of anhydrous sodium acetate at 95° gave the 3β-acetate (as II; R = Ac) (8%) [unaccompanied by the epimeric 3α-acetate or the tertiary acetate (as III; R = Ac)] and the A-nor-5α-cholest-8-ene (as IV) (90%); possibly the poor nucleophilic power of the acetate ion is responsible for the absence of the tertiary acetate (as III; R = Ac), the cationic precursor of which co-ordinates with an acetate ion less rapidly than it eliminates a proton to afford the hydrocarbon (as IV).

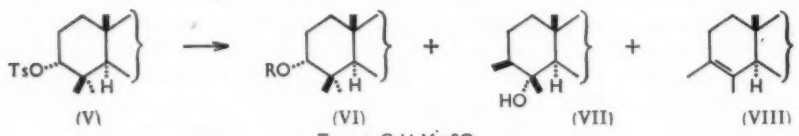
4,4-Dimethyl-5α-cholestan-3β-yl toluene-*p*-sulphonate (I) in refluxing aqueous acetone in the presence of sodium acetate afforded the 3β-alcohol (II; R = H) (5%), the tertiary



(I) (II) (III) (IV)

alcohol (III; R = H) (24%), and an apparently homogeneous A-nor-5α-cholestane (IV) (70%). The hydrocarbon (IV) was also obtained from 4,4-dimethyl-5α-cholestan-3β-ol (II; R = H) by dehydration with phosphorus pentachloride, and from the tertiary alcohol (III; R = H) by dehydration with phosphoryl chloride in pyridine. Use of acetic acid in the presence of anhydrous sodium acetate gave the 3β-acetate (II; R = Ac) (10%) and the A-nor-5α-cholestane (IV) (88%).

Since our work began, experimental analogies have become available. Moriarty and Wallis[7] established that in aqueous acetone 4,4-dimethylcholest-5-en-3β-yl toluene-*p*-sulphonate (cf. I) afforded the Δ^5-analogues of compounds (II; R = H), (III; R = H), and (IV with double-bond isomerides) in yields of 7·5%, 22·5%, and 70%, respectively. Haddad and Summers,[8] by the same reaction, obtained the Δ^5-analogue of (II; R = H) (16%), an isomeric alcohol, m. p. 126°, $[\alpha]_D$ −25° (24%) {which they regarded as 4,4-dimethyl-3,5-cyclocholestan-6β-ol though it is identical with the Δ^5-analogue of (III; R = H), m. p. 125—126°, $[\alpha]_D$ −22°, of Moriarty and Wallis}, and the Δ^5-analogue of (IV) (60%). Haddad and Summers also examined the acetolysis of 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3β-yl toluene-*p*-sulphonate (cf. I), which gave the $\Delta^{8,24}$-analogues of



(V) (VI) (VII) (VIII)

Ts = *p*-C_6H_4Me·SO_2.

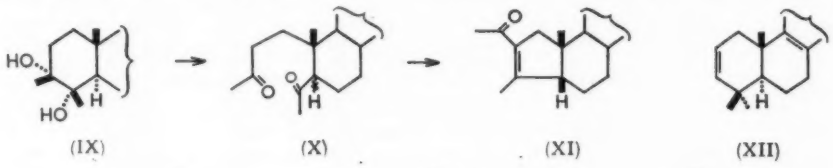
(II; R = Ac) and (IV) in 19% and 82% yield, respectively. Biellmann and Ourisson,[9] heating 4,4-dimethyl-5α-cholestan-3β-yl toluene-*p*-sulphonate (I) in aqueous acetone in the presence of calcium carbonate, obtained the A-nor-alcohol (III; R = H) (whose structure and configuration at positions 3 and 5 they proved by an unambiguous partial synthesis), and the A-nor-5α-cholestane (IV). Lastly, Atwater,[10] by methanolysis of 17β-acetoxy-4,4-dimethylandrost-5-en-3β-yl toluene-*p*-sulphonate (cf. I) in the presence of potassium acetate, obtained the corresponding 3β-alcohol (as II) (11%), the tertiary methyl ether (as III; R = Me) (29%), and the A-nor-5α-androstane (as IV), together with (probably) the isopropenyl and endocyclic isomerides (38%).

[7] Moriarty and Wallis, *J. Org. Chem.*, 1959, **24**, 1274, 1987.
[8] Haddad and Summers, *J.*, 1959, 769.
[9] Biellmann and Ourisson, *Bull. Soc. chim. France*, 1960, 348.
[10] Atwater, *J. Amer. Chem. Soc.*, 1960, **82**, 2847.

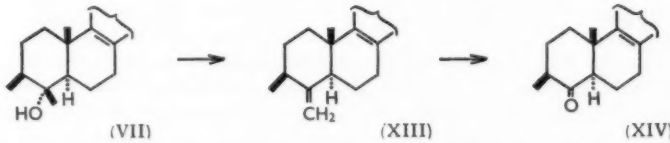
4,4,14α-Trimethyl-5α-cholest-8-en-3α-yl toluene-*p*-sulphonate (as V) in refluxing aqueous acetone in the presence of sodium acetate gave the 3α-alcohol (as VI; R = H) (7%), the tertiary alcohol (VII) (15%), and 3,4,14α-trimethyl-5α-cholesta-3,8-diene (as VIII) (75%). Acetolysis in the presence or absence of anhydrous sodium acetate in acetic acid at 95° gave the 3α-acetate (as VI; R = Ac) (17%) and the same diene (81%).

The structure of 3,4,14α-trimethyl-5α-cholesta-3,8-diene (as VIII) was proved by conversion with osmium tetroxide into the 3α,4α-glycol (as IX), which was oxidised with periodic acid to the 3,4-seco-3,4-diketone (as X), this being cyclized by aluminium oxide [11] to 2-acetyl-3,14α-dimethyl-A-nor-5β-cholesta-2,8-diene (as XI). The spectral characteristics of this compound, $\lambda_{max.}$ 1665 cm.$^{-1}$, $\nu_{max.}$ 260 mμ, and analogy with 1-acetyl-2-methylcyclopent-1-ene,[12] $\nu_{max.}$ 260 mμ, strongly support the αβ-unsaturated ketonic structure assigned (XI). Configuration at position 5 is indeterminate in the diketone (X) and regarded as β in the final product (XI).

Surprisingly, ionic dehydration of 4,4,14α-trimethyl-5α-cholest-8-en-3α-ol (as VI; R = H) with a wide variety of reagents failed to give the 3,8-diene (as VIII), and furnished



(IX) (X) (XI) (XII)



(VII) (XIII) (XIV)

in each case the isomeric 4,4,14α-trimethyl-5α-cholesta-2,8-diene [13] (XII). The 3β,4β-dimethyl-4α-hydroxy-structure (as VII) given to the tertiary alcoholic product of the solvolysis is that predicted on mechanistic grounds (see below); the equatorial 4α-hydroxyl group is supported by non-acetylation with acetic anhydride–pyridine (one week) and dehydration with phosphoryl chloride–pyridine to the 4-methylene compound (XIII), $\nu_{max.}$ (in CS_2) 885 cm.$^{-1}$, which on ozonolysis gives formaldehyde and a carbonyl compound (XIV), which could not be characterised satisfactorily. E. R. H. Jones and his colleagues [11] reported the formation of a 3-methylene compound from a 3α,4α-dimethyl-3β-hydroxy-steroid, with a tertiary equatorial hydroxyl group, by dehydration with phosphoryl chloride and pyridine.

4,4-Dimethyl-5α-cholestan-3α-yl toluene-*p*-sulphonate (as V), on solvolysis in buffered aqueous acetone, gave the 3α-alcohol (as VI; R = H) (10%), the tertiary alcohol 4α-alcohol (as VII) (15%), and 3,4-dimethyl-5α-cholest-3-ene [11] (as VIII) (72%). Acetolysis in the presence of anhydrous sodium acetate in acetic acid at 95° gave the corresponding 3α-acetate (as VI; as R = Ac) (19%) and the same hydrocarbon (VIII) (80%).

The most striking structural feature of the foregoing solvolyses is the absence of inverted unrearranged products, in contrast to the usual course of nucleophilic substitution at position 3 in saturated steroids.[14]

A kinetic study of the acetolyses of the 3-epimeric 4,4,14α-trimethyl-5α-cholest-8-en-3-yl and 4,4-dimethyl-5α-cholestan-3-yl toluene-*p*-sulphonates has been made. Selected results are given in Tables 1 and 2.

[11] Beton, Halsall, Jones, and Phillips, *J.*, 1957, 753.
[12] Schubert and Sweeney, *J. Amer. Chem. Soc.*, 1955, **77**, 2297.
[13] McGhie, Palmer, and Rosenberger, *Chem. and Ind.*, 1959, 1221.
[14] Shoppee, *J.*, 1946, 1138; Shoppee and Westcott, *J.*, 1955, 1891.

XUM

TABLE 1. *Acetolysis of* 3-*epimeric* 4,4,14α-*trimethyl*-5α-*cholest*-8-*en*-3-*yl toluene*-p-*sulphonates in anhydrous acetic acid at* 50°.

3β (a = 8·89 × 10⁻⁵ mole l.⁻¹)				3α (a = 4·37 × 10⁻⁵ mole l.⁻¹)			
Time (min.)	10^5x	log $a/(a-x)$	10^4k (min.⁻¹)	Time (min.)	10^5x	log $a/(a-x)$	10^4k (min.⁻¹)
360	0·60	0·0303	1·93	383	0·70	0·0758	4·56
1200	1·87	0·1026	1·96	845	1·41	0·1692	4·56
1290	1·99	0·1101	1·96	1035	1·65	0·2059	4·58
1930	2·84	0·1671	1·99	1320	1·95	0·2569	4·49
2850	3·86	0·2473	1·99	1455	2·10	0·2845	4·50
3500	4·45	0·3015	1·98	1895	2·50	0·3687	4·48
4000	4·90	0·3479	2·00	2230	2·78	0·4381	4·53
5000	5·60	0·4317	1·99	2380	2·86	0·4615	4·44
6000	6·21	0·5208	2·00	2744	3·08	0·5299	4·45

TABLE 2. *Acetolysis of* 3-*epimeric* 4,4-*dimethyl*-5α-*cholestan*-3-*yl toluene*-p-*sulphonates in anhydrous acetic acid at* 50°.

3β (a = 4·79 × 10⁻⁵ mole l.⁻¹)				3α (a = 2·53 × 10⁻⁵ mole l.⁻¹)			
Time (min.)	10^5x	log $a/(a-x)$	10^4k (min.⁻¹)	Time (min.)	10^5x	log $a/(a-x)$	10^4k (min.⁻¹)
407	0·89	0·0859	4·86	160	0·37	0·0686	9·87
644	1·32	0·1344	4·81	239	0·53	0·1021	9·85
933	1·78	0·1931	4·78	304	0·65	0·1289	9·78
1225	2·19	0·2530	4·75	379	0·78	0·1601	9·73
1510	2·53	0·3099	4·72	460	0·91	0·1946	9·75
1750	2·81	0·3631	4·78	543	1·04	0·2299	9·76
1970	3·03	0·4099	4·81	754	1·32	0·3203	9·78
2240	3·26	0·4651	4·79	805	1·59	0·4300	9·77
2575	3·43	0·5108	4·78	1255	1·75	0·5210	9·78

Each run was found to be kinetically of the first order, giving by use of the integrated first-order rate expression $k_1 = (1/t) \ln [a/(a-x)]$ the average specific rate constants summarised in Table 3. The increased rate in the presence of added acetate ions is of the order of magnitude expected from solvent and ionic-strength effects in acetic acid; moreover, the small increase in rate found in the presence of added lithium perchlorate

TABLE 3. *Acetolysis of* 3-*epimeric* 4,4,14α-*trimethyl*-5α-*cholest*-8-*en*-3-*yl toluene*-p-*sulphonates in acetic acid in the presence of added solutes at* 60°.

Added solute: nature	None	NaOAc		$LiClO_4$		H_2O
concn. (M)	—	0·019	0·038	0·020	0·039	0·020
10^4k_1 (min.⁻¹): 3β (0·019M)	7·4	12·2	12·7	13·5	14·2	12·8
3α (0·008M)	16·1	26·3	27·4	28·5	29·6	25·2

TABLE 4. *Acetolysis of* 4,4,14α-*trimethyl*-5α-*cholest*-8-*en*-3-*yl* (A) *and* 4,4-*dimethyl*-5α-*cholestan*-3-*yl toluene*-p-*sulphonates* (B) *in acetic acid at* 50° *and* 60°.

	3β-A	3α-A	3β-B	3α-B
10^4k_1 (min.⁻¹) at 50°	2·0	4·5	4·8	9·8
10^4k_1 (min.⁻¹) at 60°	7·4	16·1	17·1	34·2
E_A (kcal. mole⁻¹)	27·4	27·2	27·2	26·7
$\Delta H^‡$ (kcal. mole⁻¹)	26·6	26·1	26·1	25·6
$\Delta S^‡$ (kcal. mole⁻¹ deg.⁻¹)	−1·1	−1·0	−1·0	−1·1

TABLE 5. *Acetolysis of toluene*-p-*sulphonates in acetic acid at* 50°.

	Cyclohexyl [15,16]	Cholest-5-en-3β-yl *	Cholest-5-en-3α-yl [17]	4,4-Dimethylcholest-5-en-3β-yl [8]
10^4k_1 (min.⁻¹) at 50°	1·1	75·79	15·3	960
E_A (kcal. mole⁻¹)	27·9	25·0	25·2	—
$\Delta H^‡$ (kcal. mole⁻¹)	27·0	24·4	24·6	—
$\Delta S^‡$ (kcal. mole⁻¹ deg.⁻¹)	−1·1	−1·0	−3·7	—

* Davies, Meecham, and Shoppee, *J.*, 1955, 679.

is consistent with the greater degree of dissociation of this solute. Clearly, the acetolyses of the 3-epimeric 4,4,14α-trimethyl-5α-cholest-8-en-3-yl toluene-*p*-sulphonates are unimolecular reactions (S_N1) involving a rate-controlling heterolysis, and this has been found

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likewise to be true for the acetolyses of the epimeric 4,4-dimethyl-5α-cholestan-3-yl toluene-*p*-sulphonates. The sensitivity of the acetolyses of the 4,4,14α-trimethyl-5α-cholest-8-en-3-yl toluene-*p*-sulphonates towards addition of water and salts is similar to that observed with cyclohexyl [15,16] and cholest-5-en-3α-yl toluene-*p*-sulphonate.[17] The acetolysis of cholest-5-en-3β-yl toluene-*p*-sulphonate is, however, much more sensitive to addition of water and salts than that of cyclohexyl toluene-*p*-sulphonate, and it has been suggested that this is due to the greater charge separation in the transition state of the former reaction.[16]

The specific rate constants and thermodynamic functions for acetolysis of 4,4,14α-trimethyl-5α-cholest-8-en-3-yl and 4,4-dimethyl-5α-cholestan-3-yl toluene-*p*-sulphonates are given in Table 4. These rate constants are only slightly greater than that $10^4k_1 = 1{\cdot}1$ min.$^{-1}$ for cyclohexyl toluene-*p*-sulphonate in acetic acid at 50° (cf. Table 5),[15,16] and are not very different from those, $10^4k_1 = 0{\cdot}65$ min.$^{-1}$ for 5α-cholestan-3β-yl toluene-*p*-sulphonate and $10^4k_1 = 4{\cdot}4$ min.$^{-1}$ for 5α-cholestan-3α-yl toluene-*p*-sulphonate in acetic acid at 50° (Winstein, personal communication). Apart from any effect possibly due to the 14α-methyl group, comparison of the specific rate constants for the respective Δ^8-4,4-14α-trimethyl and saturated 4,4-dimethyl epimers shows that the 8,9-ethylenic linkage exerts a long-range effect, causing an approximately 50% depression in rate.[18]

The specific rate constants for the acetolyses of the 3-epimeric 4,4,14α-trimethyl and 4,4-dimethyl toluene-*p*-sulphonates are only slightly greater than that for cyclohexyl toluene-*p*-sulphonate, whilst the activation parameters are remarkably similar in all five cases. Although quite small rate increases (ten-fold or less) have been attributed to neighbouring-group participation,[19] it appears that the slight increases now found are not due to such participation by the electrons of the 4,5-bond in the 3β-compounds, or of the 4β-methyl group in the 3α-derivatives.

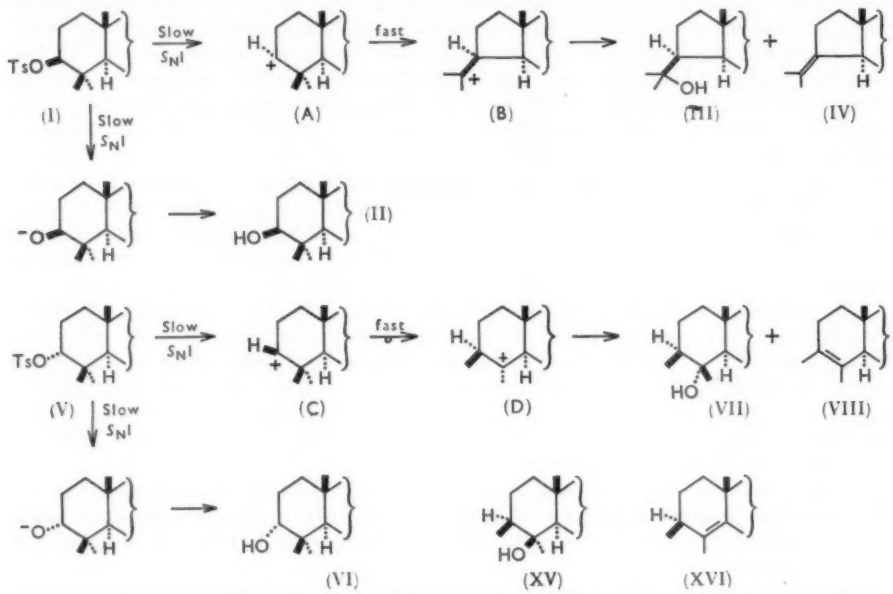
It may be noted that the enhanced rates of acetolysis of cholest-5-en-3β-yl and 4,4-dimethylcholest-5-en-3β-yl toluene-*p*-sulphonates (Table 5) are due to differences in the heats of activation ($\Delta H^{\ddagger}$), since the entropies of activation ($\Delta S^{\ddagger}$) have a nearly constant value of $-$ ~1 kcal. mole^{-1} deg.$^{-1}$.

The mechanism of solvolysis of the 3-epimeric 4,4,14α-trimethyl-5α-cholest-8-en-3-yl and 4,4-dimethyl-5α-cholestan-3-yl toluene-*p*-sulphonates (as I, V) must account (*a*) for the absence of inversion without rearrangement and the presence of some retention, and (*b*) for the absence of synartetic acceleration and the presence of some steric acceleration, in all four cases. Solvolysis may proceed by a slow unimolecular heterolysis (S_N1) to give the classical carbonium ions (A, C); since individuality is maintained, these probably exist as intimate ion-pairs with the departing toluene-*p*-sulphonate anions; they are short-lived and rapidly rearrange, before co-ordination with an external anion or depolarisation can occur, to the more thermodynamically stable carbonium ions (B, D), yielding rearranged tertiary alcohols (as III, VII) and unsaturated hydrocarbons (as IV, VIII). The occurrence of substitution with retention to afford the alcohols (as II, VI) would then be due to fission of the oxygen–sulphur bond R·O$^{+}_{!}$–SO_2Ar as opposed to the usual carbon–oxygen cleavage R$^{+}_{!}$–O·SO_2Ar. In fact such oxygen–sulphur fission can arise if the carbon–oxygen heterolysis becomes sufficiently difficult; thus Bunton and Frei [20] showed by use of isotopic oxygen that hydrolysis of phenyl toluene-*p*-sulphonate in alkaline aqueous dioxan with water enriched in ^{18}O occurred by oxygen–sulphur fission: *p*-Tol·$SO_2^{+}_{!}$–OPh + $^{18}OH^-$ ⟶ *p*-Tol·SO_2·^{18}OH + Ph·OH. However, the products isolated from the acetolyses are the acetates (II, VI; R = Ac), corresponding to the original toluene-*p*-sulphonates, and not the alcohols (II, VI) predicted by this mechanism. Further, it is difficult to explain the absence of the 4-epimeric alcohols (as XV) and the double-bond isomers (as XVI) from the products

[15] Winstein, Grunwald, and Ingraham, *J. Amer. Chem. Soc.*, 1948, **70**, 821.
[16] Winstein and Adams, *J. Amer. Chem. Soc.*, 1948, **70**, 838.
[17] Shoppee and Williams, *J.*, 1955, 686.
[18] Cf. Barton, McCapra, May, and Thudium, *J.*, 1960, 1297.
[19] Cf. Bethell and Gold, *Quart. Rev.*, 1958, **12**, 173.
[20] Bunton and Frei, *J.*, 1951, 1872.

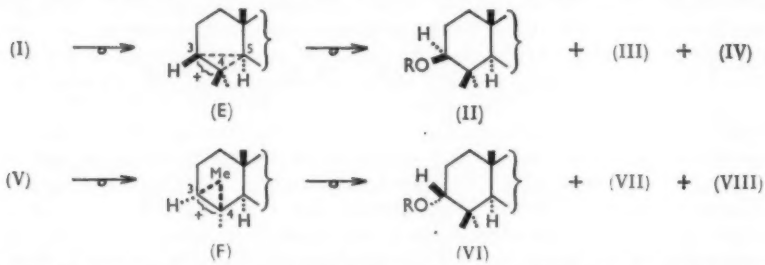
of solvolysis of the 3α-yl toluene-*p*-sulphonates (as V) if the carbonium ion (D) exists as a single classical entity.

Both these difficulties disappear if non-classical carbonium ions (E, F) (or intimate ion pairs) are postulated, and the following reaction mechanism involving them is in agreement with all the structural evidence. Thus the carbonium ions (E, F) are formed with



inversion at position 3,* and attack by a hydroxyl ion or an acetate ion at position 3 leads by a second inversion to the alcohols or acetates (as II, VI; R = H or Ac) with preservation of configuration.

The kinetic evidence requires one further assumption. Generation of the non-classical



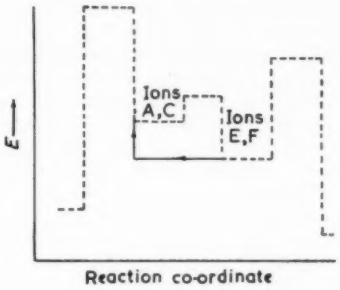
ions (E, F) in preference to the classical ions (A, C) is intelligible if the former are thermodynamically more stable; this would involve stabilised transition states of ionisation, and therefore accelerated unimolecular heterolyses. The solvolysis rates are effectively not accelerated, and the above mechanism must be modified by postulating that the rate-controlling ionisation produces classical carbonium ions (A, C) (as intimate ion-pairs) of short life, rearranging to the more stable non-classical carbonium ions (E, F), the timing of the covalency changes being such that formation of the latter does not kinetically affect

* There is a mechanistic inversion, but no formal inversion, in the process (I ⟶ III) because the 3-hydrogen atom does not cross the plane of the five-membered ring.

the initial ionisation. On this interpretation, the situation is illustrated by the broken-line portion of the symbolic energy diagram given by Ingold [21] and reproduced in the annexed Figure, subject only to the qualification that the difference in height between the left-hand and the right-hand energy barrier is insufficient to prevent return over the left-hand barrier by the combined full-line and broken-line route.

Reaction co-ordinates.

Representative points entering from the left and leaving by the right describe by the broken-line route the non-accelerated unimolecular rearrangements I ⟶ III + IV *and* V ⟶ VII + VIII. *Points entering from the left by the broken-line route, and leaving by the left by the combined full-line and broken-line route describe the non-accelerated, non-rearranging unimolecular reactions* I ⟶ II *and* V ⟶ VI.



Experimental

For general experimental directions see *J.*, 1959, 345. $[\alpha]_D$ refer to chloroform solutions at room temperature. Ultraviolet absorption spectra were determined for ethanol solutions in a Hilger Uvispec spectrophotometer. Infrared absorption spectra were measured by use of a Perkin–Elmer model 137 Infracord double-beam spectrometer. Unless otherwise stated, aluminium oxide used was Spence's type H (activity II). M. p.s were determined on a Kofler block and are corrected.

4,4,14α-*Trimethyl*-5α-*cholest*-8-*en*-3β-*yl Toluene*-p-*sulphonate*.—To a solution of 4,4,14α-trimethyl-5α-cholest-8-en-3β-ol [22] (1·02 g.) in dry pyridine (50 c.c.), toluene-*p*-sulphonyl chloride (2·60 g.) was added gradually at 0°. After 3 days at 25°, ice was added and the mixture set aside for 1·5 hr. The product was extracted with ether, and the extract washed with cold 2N-hydrochloric acid, water, 2N-sodium hydrogen carbonate, and to neutrality with water, dried, and evaporated. The solid residue (1·19 g.) gave, after several recrystallisations from acetone, **4,4,14α-*trimethyl*-5α-*cholest*-8-*en*-3β-*yl toluene*-p-*sulphonate***, m. p. 125—126°, $[\alpha]_D$ +54° (*c* 0·9) [Found (after drying at 60°/0·2 mm. for 3 hr.): C, 76·2; H, 10·0. $C_{37}H_{58}O_3S$ requires C, 76·2; H, 10·0%]. The ester (50 mg.) was eluted unchanged (m. p. 124—126°; 45 mg.) from neutralised aluminium oxide (1·5 g.; Woelm) by benzene–pentane (1 : 2).

Solvolysis of **4,4,14α-*Trimethyl*-5α-*cholest*-8-*en*-3β-*yl Toluene*-p-*sulphonate***.—A solution of 4,4,14α-trimethyl-5α-cholest-8-en-3β-yl toluene-*p*-sulphonate (1·285 g.) in acetone (25 c.c.) was treated with water (7 c.c.) and anhydrous sodium acetate (1·0 g.) and refluxed for 60 hr. Most of the acetone was removed under reduced pressure, and the residue extracted with ether, and worked up in the usual way to give a solid (930 mg.). Chromatography on aluminium oxide (30 g.) prepared in pentane and elution with pentane (4 × 80 c.c.) gave 3-isopropylidene-14α-methyl-A-nor-5α-cholest-8-ene [23] (652 mg., 72%), m. p. 145—146°, $[\alpha]_D$ +67° (*c* 0·7), after crystallisation from chloroform–methanol. Elution with ether–pentane (1 : 19; 10 × 80 c.c.) afforded **3β-(1-*hydroxy*-1-*methylethyl*)-14α-*methyl*-A-*nor*-5α-*cholest*-8-*ene*** (214 mg., 22%), m. p. 137—138° (from methanol), $[\alpha]_D$ +52° (*c* 0·9) [Found (after drying at 80°/0·2 mm. for 16 hr.): C, 83·8; H, 12·3. $C_{30}H_{52}O$ requires C, 84·0; H, 12·3%]; treatment with acetic anhydride and pyridine at 25° for 1 week failed to bring about acetylation. Further elution with ether–pentane (1 : 4; 10 × 80 c.c.) gave 4,4,14α-trimethyl-5α-cholest-8-en-3β-ol (48 mg., 5%), m. p. 145—146°, $[\alpha]_D$ +62° (*c* 0·6), after crystallisation from benzene–methanol, unaccompanied by the epimeric 3α-alcohol.

Dehydration of **3β-(1-*Hydroxy*-1-*methylethyl*)-14α-*methyl*-A-*nor*-5α-*cholest*-8-*ene***.—The foregoing alcohol (78 mg.) in pyridine (8 c.c.) was heated at 95° for 1 hr. with freshly distilled phosphoryl chloride (1·5 c.c.). Dilution with water and extraction with ether gave a product,

[21] Ingold, cf. ref. 1, Fig. 36.2, p. 520.
[22] Ruzicka, Denss, and Jeger, *Helv. Chim. Acta*, 1945, **28**, 759.
[23] Dorée, McGhie, and Kurzer, *J.*, in the press.

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which was chromatographed on aluminium oxide (3 g.) prepared in pentane. Elution with pentane (50 c.c.) and two crystallisations of the product from chloroform–methanol gave 3-isopropylidene-14α-methyl-A-nor-5α-cholest-8-ene (43 mg.), m. p. 145—146°, $[\alpha]_D$ +66° (*c* 0·9).

Acetolysis of 4,4,14α-*Trimethyl*-5α-*cholest*-8-*en*-3β-*yl Toluene*-p-*sulphonate*.—This ester (504 mg.) in acetic acid (70 c.c.) containing anhydrous sodium acetate (287 mg.) was heated at 95° for 3 hr. Removal of the solvent *in vacuo*, extraction with ether, and working up in the usual way gave an oil which showed $\nu_{max.}$ 1240 cm.$^{-1}$ in carbon disulphide but no band in the 3500 cm.$^{-1}$ region and so was devoid of 4,4,14α-trimethyl-5α-cholest-8-en-3β-ol,[24] this was hydrolysed with refluxing 5% ethanolic potassium hydroxide (20 c.c.) for 1 hr. The resulting solid (355 mg.) in pentane was chromatographed on aluminium oxide (11 g.) prepared in the same solvent. Elution with pentane (2 × 80 c.c.) gave 3-isopropylidene-14α-methyl-A-nor-5α-cholest-8-ene (318 mg., 90%), m. p. 145—146°, $[\alpha]_D$ +67° (*c* 0·7), after crystallisation from chloroform–methanol. Further elution with pentane and later benzene yielded only traces of material, whilst use of ether–benzene (1 : 99; 2 × 80 c.c.) afforded 4,4,14α-trimethyl-5α-cholest-8-en-3β-ol (32 mg., 8%), m. p. 145—146°, $[\alpha]_D$ +63° (*c* 1·0), after crystallisation from benzene–methanol, unaccompanied by the epimeric 3α-alcohol. Similar results were obtained in a second experiment without the sodium acetate buffer.

4,4-*Dimethyl*-5α-*cholestan*-3β-*yl Toluene*-p-*sulphonate*.—4,4-Dimethyl-5α-cholestan-3β-ol [25] (200 mg.) in dry pyridine (5 c.c.) was treated at 0° with toluene-*p*-sulphonyl chloride (470 mg.) and left at 25° for 3 days. The solid product (310 mg.), after several recrystallisations from acetone, yielded the *toluene*-p-*sulphonate*, m. p. 125—126°, $[\alpha]_D$ +7° (*c* 1·3) [Found (after drying at 60°/0·2 mm. for 3 hr.): C, 75·8; H, 10·2. $C_{38}H_{58}O_3S$ requires C, 75·7; H, 10·2%]. The ester (50 mg.) was eluted unchanged (m. p. 124—125°; 43 mg.) from neutralised aluminium oxide (1·5 g., Woelm) by benzene–pentane (1 : 2).

Solvolysis of 4,4-*Dimethyl*-5α-*cholestan*-3β-*yl Toluene*-p-*sulphonate*.—4,4-Dimethyl-5α-cholestan-3β-yl toluene-*p*-sulphonate (252 mg.) in acetone (10 c.c.) was refluxed with water (1 c.c.) and anhydrous sodium acetate (200 mg.) for 60 hr. Working up in the usual way gave an oil (180 mg.). Chromatography on aluminium oxide (6 g.) prepared in pentane, and elution with pentane (6 × 15 c.c.), gave an oil (123 mg., 70%) which yielded, by crystallisation from chloroform–methanol, 3-*isopropylidene*-A-*nor*-5α-*cholestane*, m. p. 87—89°, $[\alpha]_D$ +18° (*c* 1·0) [Found (after drying at 35°/0·2 mm. for 8 hr.): C, 87·25; H, 12·8. $C_{29}H_{50}$ requires C, 87·4; H, 12·6%]. The isopropenyl and endocyclic isomerides may have been present in this material. Elution with ether–pentane (1 : 19; 10 × 15 c.c.) gave 3β-(1-hydroxy-1-methylethyl)-A-nor-5α-cholestane (44 mg., 24%), m. p. 100—101° (from methanol), $[\alpha]_D$ +31° (*c* 1·0). Biellmann and Ourisson [10] give m. p. 102°, $[\alpha]_{600}$ +27°, $[\alpha]_{400}$ +69°. Elution with ether–pentane (1 : 4; 7 × 15 c.c.) gave 4,4-dimethyl-5α-cholestan-3β-ol (9 mg., 5%), m. p. 156—157°, $[\alpha]_D$ +13° (*c* 0·6), after crystallisation from methanol, unaccompanied by the epimeric 3α-alcohol.

Acetolysis of 4,4-*Dimethyl*-5α-*cholestan*-3β-*yl Toluene*-p-*sulphonate*.—The toluene-*p*-sulphonate (260 mg.) in acetic acid (35 c.c.) containing anhydrous sodium acetate (150 mg.) was heated at 95° for 3 hr. The product which had $\nu_{max.}$ (in CS_2) at 1240 cm.$^{-1}$ but no band in the 3500 cm.$^{-1}$ region and was devoid of 4,4-dimethyl-5α-cholestan-3β-ol, was hydrolysed with 5% ethanolic potassium hydroxide (10 c.c.), and the resulting oil was chromatographed on aluminium oxide (6 g.) prepared in pentane. Elution with pentane (3 × 50 c.c.) gave 3-isopropylidene-A-nor-5α-cholestane (167 mg., 88%) which, crystallised from chloroform–methanol, had m. p. 87—89°, $[\alpha]_D$ +19° (*c* 1·0). Elution with ether–pentane (1 : 4; 4 × 50 c.c.) gave 4,4-dimethyl-5α-cholestan-3β-ol (19 mg., 10%), m. p. 156—157°, $[\alpha]_D$ +11° (*c* 0·93) after crystallisation from methanol, unaccompanied by the epimeric 3α-alcohol.

3-*Isopropylidene*-A-*nor*-5α-*cholestane*.—(*a*) 4,4-Dimethyl-5α-cholestan-3β-ol (125 mg.) in hexane (10 c.c.) was heated under reflux with phosphorus pentachloride (125 mg.) for 10 min. Dilution with ice-water, extraction with ether, and working up in the usual way gave a yellow oil. Filtration through aluminium oxide (0·5 g. in pentane, 20 c.c.) and removal of the solvent *in vacuo* afforded an oil, which by repeated crystallisation from chloroform–methanol gave 3-isopropylidene-A-nor-5α-cholestane as needles, m. p. 88—90°, $[\alpha]_D$ +19° (*c* 0·8).

(*b*) To a solution of 3β-(1-hydroxy-1-methylethyl)-A-nor-5α-cholestane, 35 mg.) in pyridine

[24] Marker and Wittle, *J. Amer. Chem. Soc.*, 1937, **59**, 2289; Allsop, Cole, White, and Willix, *J.*, 1956, 4868.

[25] Mazur and Sondheimer, *J. Amer. Chem. Soc.*, 1958, **80**, 5220.

(2 c.c.), freshly distilled phosphoryl chloride (0·5 c.c.) was added. After 1 hr. at 95°, the mixture was cooled and ice-water cautiously added. Extraction with ether and working up in the usual way gave 3-isopropylidene-A-nor-5α-cholestane, m. p. 88—90°, $[\alpha]_D$ +19° (*c* 1·1), after repeated crystallisation from chloroform–methanol.

4,4,14α-Trimethyl-5α-cholest-8-en-3α-yl Toluene-p-sulphonate.—4,4,14α-Trimethyl-5α-cholest-8-en-3α-ol [24] (104 mg.) in dry pyridine (5 c.c.) was treated at 0° with toluene-*p*-sulphonyl chloride (264 mg.) and left at 25° for 3 days. The solid product (118 mg.) afforded, after several recrystallisations from acetone, *4,4,14α-trimethyl-5α-cholest-8-en-3α-yl toluene-p-sulphonate*, m. p. 139—140° (decomp.), $[\alpha]_D$ −5° (*c* 1·0) [Found (after drying at 60°/0·2 mm. for 1 hr.): C, 76·2; H, 10·3. $C_{37}H_{58}O_3S$ requires C, 76·2; H, 10·0%].

Solvolysis of 4,4,14α-Trimethyl-5α-cholest-8-en-3α-yl Toluene-p-sulphonate.—A solution of 4,4,14α-trimethyl-5α-cholest-8-en-3α-yl toluene-*p*-sulphonate (1·247 g.) in acetone (25 c.c.) was treated with water (7 c.c.) and anhydrous sodium acetate (1·0 g.), and refluxed for 60 hr. Working up in the usual way gave a solid (871 mg.), which by chromatography on a column of aluminium oxide (30 g.) prepared in pentane and elution with pentane (4 × 80 c.c.) gave *3,4,14α-trimethyl-5α-cholesta-3,8-diene* (661 mg., 75%), m. p. 94—95°, $[\alpha]_D$ +76·5° (*c* 0·8) after crystallisation from chloroform–methanol [Found (after drying at 40°/0·2 mm. for 6 hr.): C, 87·45; H, 12·3. $C_{30}H_{50}$ requires C, 87·7; H, 12·3%]. Elution with ether–pentane (1 : 9; 6 × 80 c.c.) gave *3β,4β,14α-trimethyl-5α-cholest-8-en-4α-ol* (135 mg., 15%), m. p. 138—139°, $[\alpha]_D$ +95° (*c* 0·8), after crystallisation from aqueous ethanol [Found (after drying at 90°/0·2 mm. for 12 hr.): C, 83·8; H, 12·4. $C_{30}H_{52}O$ requires C, 84·1; H, 12·2%]. Treating 3β,4β,14α-trimethyl-5α-cholest-8-en-4α-ol with acetic anhydride–pyridine at 25° for 1 week failed to bring about acetylation. Elution with ether–pentane (1 : 4; 3 × 80 c.c.) yielded 4,4,14α-trimethyl-5α-cholest-8-en-3α-ol (65 mg., 7%) which, crystallised from acetone–methanol, had m. p. 138—139°, $[\alpha]_D$ +48° (*c* 1·1); it was not accompanied by the epimeric 3β-alcohol.

Acetolysis of 4,4,14α-Trimethyl-5α-cholest-8-en-3α-yl Toluene-p-sulphonate.—4,4,14α-Trimethyl-5α-cholest-8-en-3α-yl toluene-*p*-sulphonate (610 mg.) in acetic acid (80 c.c.) containing anhydrous sodium acetate (328 mg.) was heated at 95° for 3 hr. Removal of the solvent *in vacuo*, extraction with ether, and working up in the usual way gave a yellow oil, which had $\nu_{max.}$ (in CS_2) 1240 and 1180 cm.$^{-1}$ but no band in the 3500 cm.$^{-1}$ region and was devoid of 4,4,14α-trimethyl-5α-cholest-8-en-3α-ol; [24] it was hydrolysed with refluxing 5% ethanolic potassium hydroxide (20 c.c.) for 30 min. The resulting crystals (432 mg.) were chromatographed on aluminium oxide (12 g.) prepared in pentane. Elution with pentane (2 × 80 c.c.) gave 3,4,14α-trimethyl-5α-cholesta-3,8-diene (348 mg., 81%), m. p. 94—95°, $[\alpha]_D$ +76·5° (*c* 0·8), after crystallisation from chloroform–methanol. Elution with ether–benzene (1 : 99; 10 × 80 c.c.) yielded 4,4,14α-trimethyl-5α-cholest-8-en-3α-ol (78 mg., 17%), m. p. 138—139°, $[\alpha]_D$ +48° (*c* 1·1), after crystallisation from acetone–methanol, unaccompanied by the epimeric 3β-alcohol. Similar results were obtained in a second experiment without the sodium acetate buffer.

Dehydration of 3β,4β,14α-Trimethyl-5α-cholest-8-en-4α-ol.—3β,4β,14α-Trimethyl-5α-cholest-8-en-4α-ol (75 mg.) in pyridine (8 c.c.) was heated at 95° for 1 hr. with freshly distilled phosphoryl chloride (1·5 c.c.). Dilution with water and extraction with ether gave a product which was chromatographed on aluminium oxide (3 g.) prepared in pentane. Elution with pentane (50 c.c.) afforded *3β,14α-dimethyl-4-methylene-5α-cholest-8-ene* (35 mg.), m. p. 81—82°, $[\alpha]_D$ +83° (*c* 1·0), $\nu_{max.}$ (in CS_2) 885 cm.$^{-1}$, after crystallisation from acetone [Found (after drying at 45°/0·2 mm. for 17 hr.): C, 88·05; H, 12·25. $C_{30}H_{50}$ requires C, 87·7; H, 12·3%].

Ozonolysis of 3β,14α-Dimethyl-4-methylene-5α-cholest-8-ene.—3β,14α-Dimethyl-4-methylene-5α-cholest-8-ene (28 mg.) in carbon tetrachloride (10 c.c.) was treated with excess of ozonised oxygen at −15° for 30 min. The solvent was removed under reduced pressure at 0° and water (10 c.c.) added to the residue. Most of this solution was distilled into a solution of 2,4-dinitrophenylhydrazine (300 mg.) in methanol (15 c.c.) containing hydrochloric acid (0·5 c.c.). Addition of water and extraction with benzene gave a product which was chromatographed on neutralised aluminium oxide (0·5 g.; Woelm) prepared in benzene. Elution with ether gave formaldehyde 2,4-dinitrophenylhydrazone (7 mg.), m. p. and mixed m. p. 166°. Paper chromatography [26] (cyclohexane and No. 1 paper impregnated with dimethylformamide) showed the product to be free from other 2,4-dinitrophenylhydrazones.

3,4,14α-Trimethyl-5α-cholesta-3,8-diene.—In a series of experiments 4,4,14α-trimethyl-5α-cholest-8-en-3α-ol was treated with the following reagents: PCl_5–hexane, PCl_5–pyridine,

[26] Gasparic and Vecera, *Coll. Czech. Chem. Comm.*, 1957, **22**, 1426.

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PCl_5–$POCl_3$, $POCl_3$–pyridine, $SOCl_2$, $SOCl_2$–benzene, $SOCl_2$–pyridine, but failed to give 3,4,14α-trimethyl-5α-cholesta-3,8-diene. Chromatography of the products gave, by elution with pentane, variable quantities of oil which on crystallisation from chloroform–methanol furnished 4,4,14α-trimethyl-5α-cholesta-2,8-diene,[12] m. p. 80—82°, $[\alpha]_D$ +120° (*c* 1·0).

Oxidation of 3,4,14α-*Trimethyl-5α-cholesta*-3,8-*diene with Osmium Tetroxide.*—3,4,14α-Trimethyl-5α-cholesta-3,8-diene (319 mg.) in benzene (6 c.c.) was treated with a solution of osmium tetroxide (228 mg., 1·1 mol.) in pyridine (6 c.c.), and the mixture kept in the dark for 18 days at 25°. After removal of the solvents under reduced pressure, the residue was heated under reflux with benzene (9 c.c.), methanol (9 c.c.), ethanol (9 c.c.), water (5 c.c.), mannitol (1·85 g.), and potassium hydroxide (1·85 g.). After 3½ hr. sodium sulphite (320 mg.) was added and the heating continued for a further 2 hr. Removal of the solvents under reduced pressure and extraction with ether afforded a solid which was chromatographed on aluminium oxide (10 g.) prepared in pentane. Elution with pentane (2 × 80 c.c.) afforded starting material (58 mg.). Elution with ether–pentane (1 : 9; 15 × 80 c.c.) gave 3β,4β,14α-*trimethyl-5α-cholest*-8-*ene*-3α,4α-*diol* (185 mg.), having m. p. 158—159°, $[\alpha]_D$ +70° (*c* 0·5), after crystallisation from methanol [Found (after drying at 50°/0·2 mm. for 36 hr.): C, 81·3; H, 11·6. $C_{30}H_{52}O_2$ requires C, 81·0; H, 11·8%]. Further elution with ether–pentane (1 : 9; 4 × 80 c.c.) gave material (15 mg.), m. p. 161—168° (from chloroform–methanol), probably impure 3β,4β-diol.

Oxidation of 3β,4β,14α-*Trimethyl-5α-cholest*-8-*ene*-3α,4α-*diol with Periodic Acid.*—The presumed diol (103 mg.) in dioxan (10 c.c.) was treated with periodic acid (125 mg.) in water (1 c.c.) for 25 hr. in the dark at 20°. Dilution with water, extraction with ether, and working up in the usual way gave a yellow oil (98 mg.). Chromatography on silica gel (10 g.) prepared in pentane, and elution with ether–pentane (1 : 19; 8 × 40 c.c.), gave 3,4,14α-*trimethyl*-3,4-*seco*-5α-*cholest*-8-*ene*-3,4-*dione* (83 mg.), m. p. 149—150°, $[\alpha]_D$ +83° (*c* 1·25), $\nu_{max.}$ (in CCl_4) 1710 cm.$^{-1}$, after crystallisation from methanol [Found (after drying at 60°/0·2 mm. for 3 hr.): C, 81·6; H, 11·5. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%].

2-*Acetyl*-3,14α-*dimethyl*-A-*nor*-5α-*cholesta*-2,8-*diene.*—The preceding diketone (40 mg.) in pentane (3 c.c.) was adsorbed on aluminium oxide (10 g.) (cf. ref. 11). Elution after 2 hr. with benzene gave 2-*acetyl*-3,14α-*dimethyl*-A-*nor*-5α-*cholesta*-2,8-*diene*, m. p. 124—125°, $\lambda_{max.}$ 260 mμ, $\nu_{max.}$ (in CCl_4) 1665 cm.$^{-1}$ (after crystallisation from aqueous methanol) [Found (after drying at 60°/0·2 mm. for 3 hr.): C, 84·35; H, 11·6. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%].

4,4-*Dimethyl-5α-cholestan*-3α-*ol.*—4,4-Dimethyl-5α-cholestan-3-one[11] (1·003 g.) in dry propan-2-ol (100 c.c.) was refluxed for 6 hr. in the presence of aluminium isopropoxide (1·0 g.). The mixture was then slowly distilled until the distillate was free from acetone (3 hr.). The mixture was next poured into water (100 c.c.) and ether (100 c.c.), shaken, and acidified with dilute hydrochloric acid. Working up in the usual way gave crystals (998 mg.) which were chromatographed on aluminium oxide (30 g.) prepared in pentane. Elution with ether–pentane (1 : 19; 16 × 80 c.c.) gave 4,4-*dimethyl-5α-cholestan*-3α-*ol* (348 mg.), m. p. 152—153°, $[\alpha]_D$ +5° (*c* 1·0), $\nu_{max.}$ (in CS_2) 3640, 1060, 975 cm.$^{-1}$, after crystallisation from methanol [Found (after drying at 60°/0·2 mm. for 24 hr.): C, 83·4; H, 12·65. $C_{29}H_{52}O$ requires C, 83·6; H, 12·6%]. Treatment with acetic anhydride–pyridine overnight at 25° afforded 4,4-*dimethyl*-5α-*cholestan*-3α-*yl acetate*, m. p. 146—147°, $[\alpha]_D$ −8° (*c* 1·1), $\nu_{max.}$ (in CS_2) 1240, 1180, 1035, 1010, 965 cm.$^{-1}$, after crystallisation from methanol [Found (after drying at 60°/0·2 mm. for 4 hr.): C, 81·3; H, 11·8. $C_{31}H_{54}O_2$ requires C, 81·2; H, 11·9%]. Further elution with ether–pentane (1 : 19; 6 × 80 c.c.; and 1 : 9, 23 × 80 c.c.) yielded 4,4-dimethyl-5α-cholestan-3β-ol (638 mg.), m. p. 157—158°, $[\alpha]_D$ +12° (*c* 1·8), $\nu_{max.}$ (in CS_2) 3640, 1025 cm.$^{-1}$, after crystallisation from methanol.

4,4-*Dimethyl-5α-cholestan*-3α-*yl Toluene*-p-*sulphonate.*—4,4-Dimethyl-5α-cholestan-3α-ol (200 mg.) in dry pyridine (5 c.c.) was treated at 0° with toluene-*p*-sulphonyl chloride (470 mg.) and left at 25° for 3 days. The product (298 mg.), on recrystallisation from acetone, gave 4,4-*dimethyl-5α-cholestan*-3α-*yl toluene*-p-*sulphonate*, m. p. 158—159° (decomp.), $[\alpha]_D$ −10° (*c* 1·0) [Found (after drying at 60°/0·2 mm. for 3 hr.): C, 75·8; H, 10·3. $C_{36}H_{58}O_3S$ requires C, 75·7; H, 10·2%].

Solvolysis of 4,4-*Dimethyl-5α-cholestan*-3α-*yl Toluene*-p-*sulphonate.*—A solution of 4,4-dimethyl-5α-cholestan-3α-yl toluene-*p*-sulphonate (128 mg.) in acetone (5 c.c.) was treated with water (0·7 c.c.) and anhydrous sodium acetate (0·1 g.), and refluxed for 60 hr. The product was chromatographed on aluminium oxide (3 g.) prepared in pentane. Elution with pentane (4 × 10 c.c.) gave 3,4-dimethyl-5α-cholest-3-ene (65 mg., 72%), m. p. 105—106°,

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$[\alpha]_D$ +8° (*c* 1·1), after crystallisation from acetone. Beton *et al.*[11] report m. p. 106·5—108°, $[\alpha]_D$ +5° (*c* 0·57). Elution with ether–pentane (1 : 9; 5 × 10 c.c.) gave 3β,4β-*dimethyl-5α-cholestan-4α-ol* (14 mg., 15%), m. p. 145—147°, after crystallisation from methanol [Found (after drying at 60°/0·2 mm. for 18 hr.): C, 83·75; H, 12·5. $C_{29}H_{52}O$ requires C, 83·6; H, 12·6%]. Further elution with ether–pentane (1 : 4; 6 × 10 c.c.) afforded 4,4-dimethyl-5α-cholestan-3α-ol (8 mg., 10%), m. p. 152—153°.

*Acetolysis of 4,4-Dimethyl-5α-cholestan-3α-yl Toluene-*p*-sulphonate.*—4,4-Dimethyl-5α-cholestan-3α-yl toluene-*p*-sulphonate (58 mg.) in acetic acid (8 c.c.) containing anhydrous sodium acetate (30 mg.) was heated at 95° for 3 hr. Removal of the solvent *in vacuo*, extraction with ether, and working up in the usual way gave an oil, which had $\nu_{max.}$ (in CS_2) 1240 and 1180 cm.$^{-1}$ but no band in the 3500 cm.$^{-1}$ region and was devoid of 4,4-dimethyl-5α-cholestan-3α-ol; it was hydrolysed with refluxing 5% ethanolic potassium hydroxide (20 c.c.) for 30 min. The product was chromatographed on aluminium oxide (1 g.) prepared in pentane. Elution with pentane (4 × 10 c.c.) gave 3,4-dimethyl-5α-cholest-3-ene (32 mg., 80%), m. p. 104—106°, $[\alpha]_D$ +9° (*c* 0·9), after crystallisation from acetone. Elution with ether–pentane (1 : 9; 5 × 10 c.c.) yielded 4,4-dimethyl-5α-cholestan-3α-ol (8 mg., 19%), m. p. 151—152°.

Kinetic Measurements.—The rates of acetolysis were studied at 50·00° ± 0·01° and at 60·00° ± 0·01°. For each run, about 50 c.c. of a solution of the toluene-*p*-sulphonate (0·005M to 0·02M, depending on solubility and rate of solution) were made up by weight in a glass-stoppered flask. Analyses were performed on 5 c.c. portions with approximately 0·02M-perchloric acid and/or sodium acetate in anhydrous acetic acid. Titrations were carried out with 5 c.c. microburettes and were conducted at a uniform room temperature. A saturated acetic acid solution of Bromophenyl Blue was used as indicator.[15]

Darkening of the solution towards the end of a run made it impossible to obtain an infinity titre. Rates were followed to approximately 70% completion, the mean deviation of the individual first-order constants in one run being within 3%.

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641. *Steroids and Walden Inversion. Part XLIX.* Further Observations on the Bromination of 5α-Cholestan-4-one.*

By C. W. SHOPPEE and RUTH E. LACK.

Monobromination of either 5α- or 5β-cholestan-4-one gives a mixture of 5-bromo-5α- and -5β-cholestan-4-one separable into its components by chromatography on silica gel. The material previously described as 3α,5-dibromo-5α-cholestan-4-one is a mixture of 3,3-dibromo-5α-cholestan-4-one and 3α-bromo-5α-cholestan-4-one. 3,3-Dibromo-5α-cholestan-4-one has been prepared from 3α-bromo-5α-cholestan-4-one, whilst 5,6β-dibromo-5α-cholestan-4-one has been made for comparison. 3,3-Dibromo-5α-cholestan-4-one is converted by hydrogen bromide into 3α,5-dibromo-5β-cholestan-4-one.

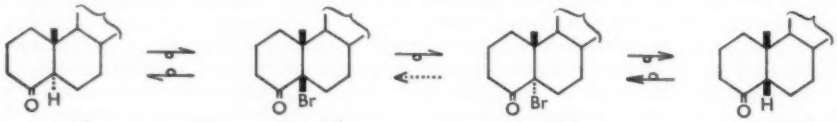
IN Part XLII,[1] monobromination of either 5α- or 5β-cholestan-4-one (I or IV) in acetic acid containing a trace of hydrogen bromide at 20° was reported to give 5-bromo-5α-cholestan-4-one (III), m. p. 145°, $[\alpha]_D$ +66°. We find that this material is a mixture separable by chromatography on silica gel into genuine 5-bromo-5α-cholestan-4-one (III), m. p. 155—157°, $[\alpha]_D$ +89°, and 5-bromo-5β-cholestan-4-one (II), m. p. 115—117°, $[\alpha]_D$ +2°. Axial bromides appear not to be the initial products of bromination,[2] and the reactions (I ⟶ II) and (IV ⟶ III) are kinetically controlled and involve inversion of configuration contrary to our previous conclusions. Reduction of the 5α-bromo-ketone (III)

* Part XLVIII, preceding paper.

[1] Shoppee, Howden, Killick, and Summers, *J.*, 1959, 630.

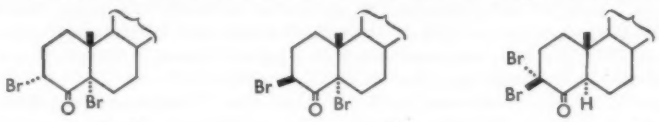
XUM

with zinc in acetic acid at 100° gives the 5β-ketone (IV) as the major product, accompanied by some of the 5α-ketone (I), probably derived from (IV) by prototropy under the conditions of reduction, since similar reduction of the 5β-bromo-ketone (II) appears to give only the 5α-ketone (I).



(I) (II) (III) (IV)

Dibromination of 5α-cholestan-4-one in acetic acid in the presence of hydrogen bromide at 20° was also reported to give a dibromo-ketone, m. p. 154°. This was regarded as 3α,5α-dibromo-5α-cholestan-4-one (V) rather than the 3β,5α-isomer (VI) because the infrared carbonyl absorption band consisted of two maxima of approximately equal intensity. The doublet could have resulted from a Fermi resonance with a higher frequency overtone, but we were impressed by the apparent analogy with the work of Allinger and Allinger,[3] who obtained curves of similar contour for the infrared carbonyl absorption band of the



(V) (VI) (VII)

equilibrium mixture in carbon tetrachloride solution of the two conformational isomers of 2-bromocyclohexanone (containing axial and equatorial bromine atoms respectively). We therefore suggested that the reputed 3α,5α-dibromo-ketone (V), which is incapable of conformational inversion, existed in carbon tetrachloride solution as an equilibrium mixture of the ring A chair (2 axial bromine atoms) and boat (1 axial and 1 equatorial bromine atom) conformations.

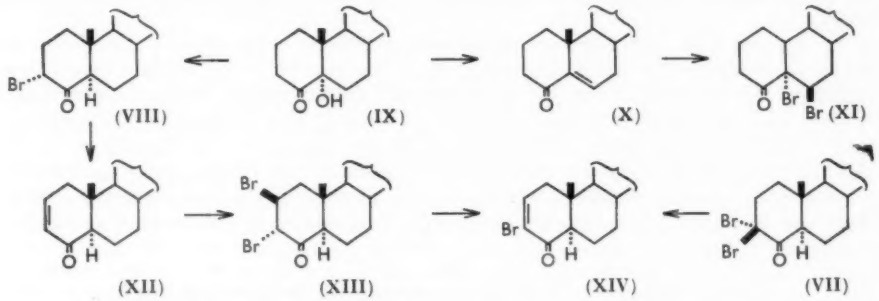
The spectral characteristics of the reputed 3α,5α-dibromo-ketone (V) have been further investigated. In the infrared region, the double peak has been found to be only slightly modified by passing from carbon tetrachloride to tetrahydrofuran as the solvent. Similarly, the ultraviolet absorption maximum at 308 mμ does not alter appreciably when the medium is changed from cyclohexane to acetonitrile. Finally, the optical rotatory dispersion curves are almost identical in cyclohexane and in acetonitrile; Professor G. Ourisson [4] writes: " in other cases, where conformational equilibria have been encountered, the change from non-polar cyclohexane to polar acetonitrile had more dramatic results than the change from cyclohexane to methanol used by Djerassi."

In brief, neither spectral (infrared, ultraviolet) nor rotatory-dispersion evidence indicates the existence of a conformational equilibrium, and we have now shown the reputed 3α,5α-dibromo-ketone (V) to be a mixture of 3,3-dibromo-5α-cholestan-4-one (VII) and 3α-bromo-5α-cholestan-4-one (VIII).

5-Hydroxy-5α-cholestan-4-one [5] (IX), which was shown to give a low yield of 3α-bromo-5α-cholestan-4-one (VIII) on prolonged treatment with hydrogen bromide in chloroform at 20°, affords the pure 3α-bromo-ketone (VIII), in almost quantitative yield, under the same conditions in 5 min. When the time is increased to 30 min., the 3α-bromo-ketone (VIII) is contaminated by an αβ-unsaturated ketone, probably cholest-5-en-4-one [5] (X). It therefore seemed possible that the reputed dibromo-ketone might be

[2] Zimmermann and Mais, *J. Amer. Chem. Soc.*, 1959, **81**, 3644; Djerassi, Finch, Cookson, and Bird, *ibid.*, 1960, **82**, 5488.
[3] Allinger and Allinger, *Tetrahedron*, 1958, **2**, 64.
[4] Ourisson, personal communication.
[5] Shoppee, Jones, Lewis, and Summers, *J.*, 1955, 2876.

derived from cholest-5-en-4-one by addition of bromine. In fact, cholest-5-en-4-one (X) readily undergoes *trans*-diaxial addition of bromine in acetic acid at 20°, but to give a



different substance, 5,6β-dibromo-5-α-cholestan-4-one (XI), exhibiting the spectral characteristics of an axial α-monobromo-ketone. The structure of 3α-bromo-5α-cholestan-4-one (VIII) is confirmed by conversion with boiling collidine under nitrogen into the αβ-unsaturated ketone 5α-cholest-2-en-4-one (XII); this adds bromine to give 2β,3α-dibromo-5α-cholestan-4-one (XIII), which is dehydrobrominated by aluminium oxide to 3-bromo-5α-cholest-2-en-4-one (XIV).

Bromination of 3α-bromo-5α-cholestan-4-one (VIII) in acetic acid in the presence of hydrogen bromide again gave the reputed 3α,5α-dibromo-ketone, m. p. 150—155°, Δν 0° and +18 cm.$^{-1}$, Δλ + 23 mμ; although fractional crystallisation or chromatography on neutral aluminium oxide was ineffective, chromatography on silica gel in pentane achieved a separation into a new compound 3,3-dibromo-5α-cholestan-4-one (VII), m. p. 179—181°, $[\alpha]_D$ −58°, Δν + 17 cm.$^{-1}$, Δλ + 20 mμ, and unaltered 3α-bromo-ketone (VIII). The *gem*-dibromo-structure (VII), with one bromine atom axial and one bromine atom equatorial, is consistent with the spectral characteristics quoted, and is proved by the rotatory dispersion curve, which shows a negative Cotton effect.[6] This circumstance excludes 3β,5-dibromo-5α-cholestan-4-one (VI), since this structure requires a positive Cotton effect.[6] The structure of 3,3-dibromo-5α-cholestan-4-one (VII) is confirmed by dehydrobromination with refluxing collidine under nitrogen to 3-bromo-5α-cholest-2-en-4-one (XIV).

Treatment of 3α-bromo-5α-cholestan-4-one (VIII) with a large excess of bromine in acetic acid in the presence of hydrogen bromide at 20° gave a product, m. p. 160—165°, unchanged by recrystallisation, exhibiting a single infrared band at 1730 cm.$^{-1}$ with a shoulder at 1713 cm.$^{-1}$, consisting of a 3 : 1 mixture of the 3,3-dibromo-ketone (VII) and the 3α-bromo-ketone (VIII), and separable into its components by chromatography on silica gel in pentane.

In an attempt to avoid acid-catalysed enolisation and possible rearrangement of the first-formed dibromo-ketone, base-catalysed bromination of 3α-bromo-5α-cholestan-4-one was examined. This method, although successfully employed [7] to afford pure 2,2-dibromo-5α-cholestan-3-one from 2α-bromo-5α-cholestan-3-one, gave after 20 hr. a product, m. p. 128—130°, $\nu_{max.}$ 1712s, 1729w cm.$^{-1}$, shown by analysis to be a 1 : 3 mixture of the 3,3-dibromo-ketone (VII) and the 3α-bromo-ketone (VIII), which could not be separated by crystallisation. Prolonged base-catalysed bromination gave a similar product, m. p. 130—135°, $\nu_{max.}$ 1712s, 1730w cm.$^{-1}$, which was separated by chromatography on silica gel in pentane into its components (VII) and (VIII).

The 3,3-dibromo-ketone (VII) and the 3α-bromo-ketone (VIII) appear to form a series of solid solutions, since bromination of the latter under varying conditions gave a series of products, incapable of separation by fractional crystallisation or by chromatography

[6] Djerassi and Klyne, *J. Amer. Chem. Soc.*, 1957, **79**, 1506.
[7] Crowne, Evans, Green, and Long, *J.*, 1956, 4351.

XUM

on neutral aluminium oxide, showing an approximately linear variation in m. p. with analytical composition [percentage of (VII) 0, 24·9, 58·9, 74·2, 100; m. p. 120°, 129°, 152°, 163°, 180°] and in the ratio of the intensities of the two infrared peaks at 1710 and 1729 cm.$^{-1}$.

It appears that dibromination of 5α-cholestan-4-one gives initially the 5α-bromo-ketone (accompanied by the 5β-bromo-ketone as a minor product), which is rapidly converted by hydrogen bromide, by reduction and rebromination under thermodynamic control, into the 3α-bromo-ketone; this then undergoes slow incomplete bromination to give the 3,3-dibromo-ketone. The sequence, 5α-Br ⟶ 3α-Br ⟶ 3,3-Br_2, in the 5α-cholestan-4-one series recalls that found, 5α-Br ⟶ 7α-Br ⟶ 7,7-Br_2, in the 5α-cholestan-6-one series;[8] we are unable to account for the absence of the 3α,5α-dibromo-4-ketone since the 5α,7α-dibromo-6-ketone (also a *cis*-2,6-dibromocyclohexanone) was obtained without difficulty.

Physical properties of the 5-cholestan-4-ones and their bromo-derivatives.

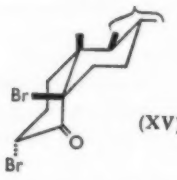
Compound	M. p.	$[\alpha]_D$	$\lambda_{max.}$ (cm.$^{-1}$)	Δλ	$\lambda_{max.}$ (mμ)	Δλ
(I) 5α-Cholestan-4-one	100°	+27°	1712	—	285	—
(IV) 5β-Cholestan-4-one	110	+40	1713	—	285	—
(II) 5α-Bromo-5α-ketone	155	+89	1713	−1	310	+25
(III) 5β-Bromo-5β-ketone	115	+2	1713	0	310	+25
(VIII) 3α-Bromo-5α-ketone	121	−72	1712	0	309	+24
(VII) 3,3-Dibromo-5α-ketone	179	−58	1729	+15	305	+20
(XV) 3α,5β-Dibromo-5β-ketone	109	—	1728	+16	309	+24

Compound	Cotton curve sign and molar amplitude ($10^{-2}a$)	Molar dispersion contribn. of subst. (Δ*a*)	Position λ* (mμ) of 1st trough (peak)	Δλ*	Halogen confign.
(I)	−94° [a]	—	307·5 [a]	—	—
(IV)	+22 [b]	—	300 [b]		
(II)	+149	+243° (5α-Br)	332	+24·5	*ax*
(III)	−213	−235 (5β-Br)	335	+35	*ax*
(VIII)	−202	−108 (3α-Br)	332	+24·5	*ax*
(VII)	−194	−100 (3α-Br)	325	+17·5	*eq*, *ax*
(XV)	−110	−132 (5β-Br)	331	+31	*eq*, *ax*

Δλ* is the difference (in mμ) between the position of the first trough (peak) of the compound and of its parent ketone.

[a] Djerassi, Closson, and Lippman, *J. Amer. Chem. Soc.*, 1956, **78**, 3163. [b] Djerassi, Riniker, and Riniker, *ibid.*, p. 6362; Mouli, Ringold, and Djerassi, *ibid.*, 1960, **82**, 5494.

Finally, extended bromination (6 days) of 3α-bromo-5α-cholestan-4-one (VIII) in anhydrous acetic acid–chloroform in the presence of hydrogen bromide at 20° afforded a new dibromo-ketone, whose spectral characteristics by comparison with those of 5α-cholestan-4-one reveal differences, Δν + 16 cm.$^{-1}$ and Δλ + 24 mμ, indicative of one axial bromine atom and one equatorial bromine atom. The compound was thought to be 3β,5-dibromo-5α-cholestan-4-one (VI), derived from the first-formed 3,3-dibromo-5α-cholestan-4-one (VII) by debromination with hydrogen bromide and rebromination,[7,9] and should then give a positive Cotton curve. The compound, however, shows a simple negative Cotton curve, and must therefore be 3α,5-dibromo-5β-cholestane (XV). The molar dispersion contribution, Δ*a* = −132°, of the axial 5β-bromine atom in compound (XV) is consistent with that found, Δ*a* = −235°, for the 5β-bromine atom in compound (III); further proof of structure by dehydrobromination was prevented by lack of material, but it is hoped to undertake this in the future. Compounds (VI) and (XV) are spectroscopically indistinguishable; their differentiation further illustrates the analytical power of optical rotatory dispersion measurements.



(XV)

[8] Shoppee, Jenkins, and Summers, *J.*, 1958, 1657.
[9] Cookson and Dandegaonkar, *J.*, 1955, 352; James and Shoppee, *J.*, 1958, 1064.

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The physical properties of the cholestan-4-ones and their bromo-derivatives are summarised in the Table.

Experimental

For general directions see *J.*, 1959, 630. $[\alpha]_D$ are for $CHCl_3$ solutions; ultraviolet absorption spectra were measured for EtOH solutions on a Hilger Uvispek spectrophotometer; infrared absorption spectra were determined for CCl_4 solutions on a Perkin–Elmer model 21 double-beam instrument or an Infrachord spectrophotometer. Analytical samples were dried at 20°/0·1 mm. for 2—4 hr.

Bromination of 5α-Cholestan-4-one.—5α-Cholestan-4-one (700 mg.), in acetic acid (100 ml.) containing a trace of hydrogen bromide, was treated at 20° with bromine (320 mg., 1·05 mol.) in acetic acid. After 10 min. water was added, and the precipitate filtered off, washed with water, and dried. The product, m. p. 122—145°, was chromatographed on Davison silica gel (100—200 mesh; W. R. Grace & Co., Baltimore, Ind., U.S.A.); the column was prepared from the silica gel (75 g.) made into a slurry with ether–pentane (1 : 19), which was then washed free from ether with pentane. Elution with pentane (3 × 30 ml.) gave *5-bromo-5β-cholestan-4-one* (120 mg.) (from methanol), m. p. 115—117° (mixed m. p. with 3α-bromo-5α-cholestan-4-one depressed to 85—90°), $[\alpha]_D$ +2°, 0° (*c* 1·0), $\nu_{max.}$ 1713 cm.$^{-1}$, $\lambda_{max.}$ 310 (log ε 1·75), rotatory dispersion: $[\alpha]_{335}$ − 1910° (trough), $[\alpha]_{288}$ + 2670° (peak) (*c* 0·01 in MeOH at 20°) (Found: C, 69·4; H, 10·0. $C_{27}H_{45}BrO$ requires C, 69·6; H, 9·7%). Further elution with ether–pentane (1 : 99, 5 × 50 ml.) gave *5-bromo-5α-cholestan-4-one* (600 mg.), m. p. 155—157°, $[\alpha]_D$ +89° (*c* 1·0), $\nu_{max.}$ 1713 cm.$^{-1}$, $\lambda_{max.}$ 310 mμ (log ε 1·9), rotatory dispersion: $[\alpha]_{332}$ +1520° (peak), $[\alpha]_{288}$ −1680° (trough) (*c* 0·01 in MeOH at 20°), after recrystallisation from acetone (Found: C, 69·35; H, 9·6%). Subsequent elution with ether–pentane (1 : 19; 2 × 50 ml.) gave unchanged 5α-cholestan-4-one (157 mg.), m. p. and mixed m. p. 99—100°.

Reduction of 5-Bromo-5α-cholestan-4-one.—5-Bromo-5α-cholestan-4-one (100 mg.) in acetic acid (20 ml.) was treated with zinc dust (200 mg.) at 100° for 2 hr. The usual isolation gave crystals, m. p. 75—85°, which were chromatographed on silica gel (10 g.). Elution with ether–pentane (2 : 98; 3 × 25 ml.) gave 5β-cholestan-4-one (52 mg.), m. p. and mixed m. p. 108—109° (from methanol). Further elution with the same solvent (2 × 25 ml.) gave material, m. p. 85—95° (19 mg.), probably a mixture of 5β- and 5α-cholestan-4-one. Yet further elution with the same solvent (2 × 25 ml.) gave 5α-cholestan-4-one (11 mg.), m. p. and mixed m. p. 98—99°.

Reduction of 5-Bromo-5β-cholestan-4-one.—5-Bromo-5β-cholestan-4-one (20 mg.) in acetic acid (10 ml.) was treated with zinc dust (40 mg.) at 100° for 2 hr. The usual working up gave 5α-cholestan-4-one (14 mg.), m. p. and mixed m. p. 98—99° (mixed m. p. with 5β-cholestan-4-one depressed to 85—89°).

3α-Bromo-5α-cholestan-4-one.—(*a*) 5-Hydroxy-5α-cholestan-4-one [5] (m. p. 158—159°; 1 g.) in chloroform (20 ml.) was treated with a stream of dry hydrogen bromide at 20° for 0·5 hr. The usual isolation procedure gave an oil, which was chromatographed on aluminium oxide (30 g.; Woelm, neutral) in pentane. Elution with pentane (6 × 25 ml.) gave 3α-bromo-5α-cholestan-4-one (220 mg.), m. p. 117—120°, $[\alpha]_D$ −75° (*c* 0·85), $\nu_{max.}$ 1713 cm.$^{-1}$, $\lambda_{max.}$ 309 mμ (log ε 2·0), after recrystallisation from acetone. Further elution with benzene–pentane gave crystalline fractions, m. p. 82—85°, with $\nu_{max.}$ 1712 (C=O), 1685 (C=C–C=O), and 1610 (C=C) cm.$^{-1}$, probably a mixture of a monobromo-ketone and an unsaturated ketone.

(*b*) The hydroxy-ketone (1 g.), as in (*a*), with hydrogen bromide for 5 min., gave 3α-bromo-5α-cholestan-4-one (1·05 g.), m. p. 121—122°, $[\alpha]_D$ −72° (*c* 0·9), $\nu_{max.}$ 1712 cm.$^{-1}$, $\nu_{max.}$ 309 mμ (log ε 2·0), rotatory dispersion: $[\alpha]_{332}$ −1770° (trough), $[\alpha]_{282}$ +2580° (peak) (*c* 0·01 in MeOH at 20°), after recrystallisation from acetone (Found: C, 69·6; H, 9·8%). Reduction with zinc in acetic acid gave 5α-cholestan-4-one (910 mg.), m. p. and mixed m. p. 100—101°, $\nu_{max.}$ 1712 cm.$^{-1}$, $\lambda_{max.}$ 285 mμ.

(*c*) 5-Bromo-5α-cholestan-4-one (m. p. 155—157°; 20 mg.) in acetic acid (5 ml.) containing a trace of hydrogen bromide was left at 20° for 0·75 hr. The usual procedure gave 3α-bromo-5α-cholestan-4-one (from acetone) (18 mg.), m. p. and mixed m. p. 117°, $[\alpha]_D$ −70° (*c* 0·85).

5α-Cholest-2-en-4-one.—3α-Bromo-5α-cholestan-4-one (1 g.) was heated with 2,4,6-collidine (20 ml.) under nitrogen at 160° for 4 hr. The customary procedure afforded an oil, which was chromatographed on aluminium oxide (30 g.) in pentane. Elution with benzene–pentane

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(1 : 4; 2 × 50 ml.) gave an oil, $\nu_{max.}$ 1712 and 1689 cm.$^{-1}$; further elution with benzene–pentane (2 : 3; 4 × 50 ml.) gave *5α-cholest-2-en-3-one* (735 mg.), double m. p. 73°/93°, $\nu_{max.}$ 1689 cm.$^{-1}$, $\lambda_{max.}$ 239 mμ (log ε 4·01), after recrystallisation from methanol (Found: C, 84·5; H, 11·8. $C_{27}H_{44}O$ requires C, 84·55; H, 11·5%).

5,6β-*Dibromo-5α-cholestan-4-one*.—Cholest-5-en-4-one [4] [100 mg., m. p. 111°, $\nu_{max.}$ 1685 cm.$^{-1}$, $\lambda_{max.}$ 241 mμ (log ε 3·9)] in acetic acid (5 ml.) was treated with bromine (42 mg., 1·06 mol.) in acetic acid (2 ml.). Decolorisation was immediate, and after 5 min. the product was poured into water and extracted with ether, to give 5,6β-*dibromo-5α-cholestan-4-one* (from ethanol) (120 mg.), m. p. 88°, $[\alpha]_D$ −13° (*c* 0·9), $\nu_{max.}$ 1712 cm.$^{-1}$, $\lambda_{max.}$ 308 mμ (Found: C, 59·8; H, 8·35. $C_{27}H_{44}Br_2O$ requires C, 59·55; H, 8·15%).

Bromination of 3α-Bromo-5α-cholestan-4-one in the Presence of Hydrogen Bromide.—(*a*) 3α-Bromo-5α-cholestan-4-one (200 mg.) in acetic acid (30 ml.) and chloroform (3 ml.) was treated with bromine (74 mg., 1·06 mol.) and a trace of hydrogen bromide at 20° for 18 hr. After removal of the excess of bromine with aqueous sodium hydrogen sulphite, the solution was worked up in the usual manner to give crystals, m. p. 140—150° (a few crystals remain at 160°). Recrystallisation from ethanol gave material (150 mg.), m. p. 150—155°, $[\alpha]_D$ −63° (*c* 0·9), $\nu_{max.}$ (in CCl_4) 1712, 1730 cm.$^{-1}$ (equal intensities), $\nu_{max.}$ (in Nujol) 1710, 1726 cm.$^{-1}$, $\lambda_{max.}$ 308 mμ, rotatory dispersion: $[\alpha]_{600}$ +25°, $[\alpha]_{500}$ +45°, $[\alpha]_{400}$ +325°, $[\alpha]_{340}$ +970°, $[\alpha]_{329}$ +500°, $[\alpha]_{308}$ −500°, $[\alpha]_{285}$ −1250°, $[\alpha]_{260}$ −1060° (*c* 0·7—0·07 in *cyclo*hexane at 20°), $[\alpha]_{600}$ +25°, $[\alpha]_{500}$ +45°, $[\alpha]_{400}$ +320°, $[\alpha]_{328}$ +920°, $[\alpha]_{327}$ +500°, $[\alpha]_{308}$ −500°, $[\alpha]_{285}$ −1250°, $[\alpha]_{260}$ −1060° (*c* 0·7—0·07 in methyl cyanide at 20°) (Found: C, 63·7; H, 8·65. Calc. for $C_{27}H_{45}BrO$: C, 69·7; H, 9·65. Calc. for $C_{27}H_{44}Br_2O$: C, 59·55; H, 8·15%). This corresponds to 50% of mono- and 50% of di-bromo-ketone, which could not be separated by recrystallisation or by chromatography on neutral aluminium oxide. This mixture (100 mg.) was chromatographed on a column of Davison silica gel (30 g.) prepared as described above. Elution with pentane (10 × 10 ml.) gave 3,3-*dibromo-5α-cholestan-4-one* (25 mg.), m. p. 179—181°, $[\alpha]_D$ −58° (*c* 0·95), $\nu_{max.}$ 1730 cm.$^{-1}$, $\lambda_{max.}$ 305 mμ (log ε 2·1), rotatory dispersion: $[\alpha]_{700}$ −543°, $[\alpha]_{325}$ −1585°, $[\alpha]_{275}$ +1920°, $[\alpha]_{262·5}$ +1736°, $[\alpha]_{255}$ +2090° (*c* 0·0249 in dioxan at 24°), after recrystallisation from acetone (Found: C, 59·25; H, 8·2. $C_{27}H_{44}Br_2O$ requires C, 59·55; H, 8·15%). Further elution with pentane containing only a few drops of ether gave a product, m. p. 150—154°, whilst elution with ether–pentane (1 : 99; 2 × 20 ml.) gave unchanged 3α-bromo-5α-cholestan-4-one (15 mg.), m. p. and mixed m. p. 119—120°, after recrystallisation from acetone.

(*b*) 3α-Bromo-5α-cholestan-4-one (100 mg.) in chloroform (2 ml.), acetic acid (20 ml.), and a trace of hydrogen bromide was treated with bromine (140 mg., 4·0 mol.) at 20° for 18 hr. The usual isolation gave crystals (92 mg.), m. p. 160—165°, $\nu_{max.}$ 1730s, 1713w cm.$^{-1}$ (Found: C, 62·15; H, 8·65%). These figures correspond to 74% of dibromo-ketone. The mixture (80 mg.) was chromatographed on silica gel, as above, to give 3,3-dibromo-5α-cholestan-4-one (from acetone) (20 mg.), m. p. and mixed m. p. 178—179°, $\nu_{max.}$ 1730 cm.$^{-1}$, $\lambda_{max.}$ 304 mμ, after recrystallisation. Further elution gave unchanged 3α-bromo-5α-cholestan-4-one (15 mg.), m. p. and mixed m. p. 119—120°, after recrystallisation from acetone.

Bromination of 3α-Bromo-5α-cholestan-4-one in the Presence of Potassium Acetate.—(*a*) 3α-Bromo-5α-cholestan-4-one (150 mg.) in acetic acid (15 ml.) containing potassium acetate (1 g.) was treated with bromine (55 mg., 1·06 mol.) at 90° for 1 hr. and 20° for 18 hr. After decolorisation with sodium hydrogen sulphite, the usual isolation gave crystals (95 mg.), m. p. 128—130°, $\nu_{max.}$ 1729w, 1712s cm.$^{-1}$ (Found: C, 67·15; H, 9·4%). This corresponds to 75% of mono- and 25% of dibromo-ketone, which could not be separated by recrystallisation.

(*b*) The product from (*a*), m. p. 128—130° (100 mg.), in acetic acid (20 ml.) was further treated with potassium acetate (1 g.) and bromine (140 mg., 4 mol.) in chloroform (5 ml.) for 24 hr. at 20°. The usual working up gave crystals (80 mg.), m. p. 130—135°, $\nu_{max.}$ 1730w, 1712s cm.$^{-1}$, which were separated by chromatography on silica gel, as previously described, into 3,3-dibromo-5α-cholestan-4-one (10 mg.), m. p. and mixed m. p. 179—180°, and unchanged 3α-bromo-5α-cholestan-4-one (25 mg.), m. p. and mixed m. p. 119—120°.

Bromination of 5-Bromo-5α-cholestan-4-one.—(*a*) 5-Bromo-5α-cholestan-4-one (m. p. 155—157°; 100 mg.) in acetic acid (30 ml.) was treated with bromine (37 mg., 1·05 mol.) and a trace of hydrogen bromide at 20° for 0·75 hr. The product, isolated by precipitation with water, had m. p. 155—160°, $\nu_{max.}$ 1728 and 1710 cm.$^{-1}$ (equal intensities), and was chromatographed on silica gel as above, to give by elution with pentane 3,3-dibromo-5α-cholestan-4-one (15 mg.), m. p. and mixed m. p. 179—180°, $\nu_{max.}$ 1729 cm.$^{-1}$, $\lambda_{max.}$ 305 mμ, after recrystallisation from

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acetone; further elution with ether–pentane (1 : 100) and recrystallisation from acetone gave 3α-bromo-5α-cholestan-4-one (15 mg.), m. p. and mixed m. p. 117—119°, $\nu_{max.}$ 1712 cm.$^{-1}$, $\lambda_{max.}$ 309 mμ.

(*b*) 5-Bromo-5α-cholestan-4-one (100 mg.) in acetic acid (50 ml.) was treated with bromine (74 mg., 2·1 mol.) at 20° for 24 hr. Addition of water gave unchanged 5-bromo-5α-cholestan-4-one (78 mg.).

(*c*) 5-Bromo-5α-cholestan-4-one (100 mg.) in acetic acid (50 ml.) was treated with 1 drop of a saturated solution of hydrogen bromide in acetic acid and then dropwise with bromine (37 mg., 1·05 mol.) and anhydrous sodium acetate (18 mg.) in acetic acid (10 ml.). After 4 hr. at 20° the bromine was not decolorised, and dilution with water gave unchanged 5-bromo-5α-cholestan-4-one (80 mg.), m. p. and mixed m. p. 154—155° (from acetone).

3-*Bromo*-5α-*cholest*-2-*en*-4-*one*.—(*a*) 5α-Cholest-2-en-4-one (50 mg.) in chloroform (20 ml.) was treated with bromine (22 mg., 1·05 mol.) in chloroform at 20°. The usual working up gave 2β,3α-*dibromo*-5α-*cholestan*-4-*one* (55 mg.) (from acetone), m. p. 185—187°, $\lambda_{max.}$ 310 mμ (log ε 1·5) (Found: C, 59·65; H, 8·0. $C_{27}H_{44}Br_2O$ requires C, 59·55; H, 8·15%). Chromatography of the 2β,3α-dibromo-ketone (500 mg.) on aluminium oxide (Spence, type H, activity ~II; 15 g.) and elution with benzene–pentane (1 : 9; 4 × 30 ml.) furnished 3-*bromo*-5α-*cholest*-2-*en*-4-*one* (345 mg.), m. p. 131—132°, $\nu_{max.}$ 1702 cm.$^{-1}$, $\lambda_{max.}$ 265 mμ (log ε 3·91), after recrystallisation from acetone (Found: C, 70·0; H, 9·15. $C_{27}H_{43}BrO$ requires C, 69·95; H, 9·35%).

(*b*) 3,3-Dibromo-5α-cholestan-4-one (50 mg.) was heated with 2,4,6-collidine (5 ml.) under nitrogen at 160° for 0·5 hr. The product, isolated in the usual way, was chromatographed on aluminium oxide (Spence, type H; 1·5 g.); elution with benzene–pentane (1 : 9) yielded 3-bromo-5α-cholest-2-en-4-one (from acetone), m. p. 131—132° alone or mixed with the sample prepared as in (*a*).

3β,5-*Dibromo*-5α-*cholestan*-4-*one*.—3α-Bromo-5α-cholestan-4-one (100 mg.) in acetic acid (20 ml.) and dry chloroform (5 ml.) was treated with bromine (55 mg., 1·5 mol.) in acetic acid (5 ml.) and a 50% solution of hydrogen bromine in acetic acid (1 ml.) for 44 hr. at 20°. After being worked up in the usual manner, the brown oil crystallised slowly from ethanol, to give 3α,5-*dibromo*-5β-*cholestan*-4-*one* (60 mg.), m. p. 109°, $\nu_{max.}$ 1728 cm.$^{-1}$, $\lambda_{max.}$ 309 mμ (log ε 1·9), optical rotatory dispersion: $[\alpha]_{700}$ 0°, $[\alpha]_{589}$ −16°, $[\alpha]_{331}$ −1730°, $[\alpha]_{314}$ 0°, $[\alpha]_{280}$ +287°, $[\alpha]_{257}$ +199° (*c* 0·075 in MeOH at 27°) (Found: C, 59·3; H, 8·1. $C_{27}H_{44}Br_2O$ requires C, 59·55; H, 8·15%). A mixed m. p. with 3α-bromo-5α-cholestan-4-one was 85—90°.

We thank Professor Guy Ourisson, University of Strasbourg, for measuring the rotatory dispersion of the reputed 3α,5-dibromo-5α-cholestan-4-one, Professor C. Djerassi, Stanford University, for measuring rotatory dispersion of the compounds (VII) and (XV), and Professor W. Klyne, Westfield College, University of London, for measuring rotatory dispersion of compounds (II), (III), and (VIII).

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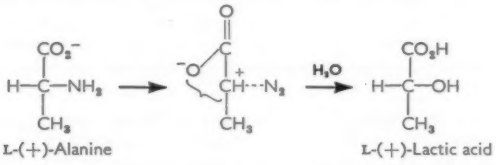
642. *The Steric Course of Lactonisation following the Deamination of Glutamic Acid, Glutamine, and γ-Aminovaleric Acid.*

By A. T. Austin and J. Howard.

The rear of the carbonium ion, formed by the action of nitrous acid on the α-amino-group of glutamine and glutamic acid, is protected against chemical attack by the α-carboxyl group and a similar interaction, by the γ-carboxyl or γ-carbamoyl group, protects the *front* of the carbonium ion. The two effects, operating together, in a spirocyclic transition state prevent other entities from reacting with the carbonium ion and account for the purity of the products formed in the two reactions.

The " front-side " interaction (based on the 80% retention of configuration of the lactone obtained when γ-aminovaleric acid was deaminated—with subsequent reaction by an S_Ni-mechanism—is derived from electrostatic interaction between the diazonium cation (the precursor of the carbonium ion) and the γ-carboxyl or γ-carbamoyl group, and constitutes a third factor conducive to the high yield of lactone when glutamine and glutamic acid are deaminated.

Hughes, Ingold, and their collaborators [1] have shown that the deamination of optically active alanine by nitrous acid gives an optically active lactic acid with retention of configuration. To explain this they postulate that the α-carboxylate group " holds " the configuration of the carbonium ion in much the same way as they suggested to account for retention in the unimolecular hydrolysis of optically active halogeno-acid ions. The α-carboxylate group is depicted as holding the carbonium ion in a pyramidal configuration until the incoming group enters the position originally occupied by the amino-group:



L-(+)-Alanine L-(+)-Lactic acid

If this happens it could influence the chemical course of the reaction because the carboxylate group should protect the rear of the carbonium ion against chemical attack. The purity of the products obtained in the deamination of glutamic acid and glutamine (nitrogen and 93% of lactone) indicates that the carbonium ion, which is formed by the action of nitrous acid on the α-amino-group, is strongly shielded against interaction with nitrite ions and solvent molecules. The present investigation has shown that in γ-amino-acids an interaction similar to that of the α-carboxylate group comes into play on the *other* side of the carbonium ion centre and shields the front of the carbonium ion.

In the absence of an α-carboxylate group the Hughes–Ingold school observed overall inversion of configuration (with much racemisation) in the deamination of simple optically active amines and explained this as due to a symmetrical shielding of the carbonium ion by the extruded nitrogen. It has been shown [2] that when the α-carboxyl group in αγ-dicarboxy-amines is replaced by the less polar hydrogen or methyl less lactone is formed on deamination and it was desirable to ascertain the steric course of lactonisation during deamination of γ-carboxy-amines where the configuration-holding effect of the α-carboxylate group is absent.

[1] Brewster, Hiron, Hughes, Ingold, and Rao, *Nature*, 1950, **166**, 179.
[2] Austin and Howard, *J.*, in the press.

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Results

Deamination of L-(+)-*Glutamic Acid and* L-(+)-*Glutamine.*—Deamination of each of these compounds gave a lævorotatory hydroxy-acid. As a lactone is an isolable intermediate the results obtained may be depicted:

L-(+)-Glutamine ⟶ Lactone ⟶ (−)-α-Hydroxyglutarate
$[\alpha]_D^{21}$ + 6·75° (in H_2O) $[\alpha]_D^{21}$ −7·5° (in aq. NaOH)

L-(+)-Glutamic acid ⟶ Lactone ⟶ (−)-α-Hydroxyglutarate
$[\alpha]_D^{18}$ +29·6° (in 5% HCl) $[\alpha]_D^{21}$ −9·2° (in aq. NaOH)

Deamination of (+)-γ-*Aminovaleric Acid.*—The lactone formed in the deamination of this compound was extracted with ether and purified and its optical rotation measured. The lactone was then hydrolysed to the hydroxy-acid and the optical rotation measured.

(+)-γ-Aminovaleric acid ⟶ (−)-γ-Valerolactone ⟶ (+)-Hydroxyvaleric acid
$[\alpha]_D^{22}$ +12° $[\alpha]_D^{22}$ −13·7° $[\alpha]_D^{22}$ +6°

The configuration of (+)-γ-aminovaleric acid was related to that of (+)-β-aminobutyric acid which was related to (+)-α-alanine by processes that did not involve breaking any of the bonds attached to the asymmetric carbon centre: when these amino-acids have the same sign of optical rotation they have the same configuration:

(+)-γ-aminovaleric acid ~ (+)-β-aminobutyric acid ~ (+)-α-alanine
(the symbol ~ means " corresponds in configuration to ")

During our work identical configurational relations have been reported for the second correlation by Fuks [3] and for the overall relation by Balenovic and Cerar.[4]

Discussion

The formation of the same lævorotatory hydroxy-acid * on the deamination of L-glutamic acid and L-glutamine shows that the steric course of the reaction leading to the lactone must also be the same. It has been established [6] that these acids give the same lactone (γ-carboxy-γ-butyrolactone) in the same amount, so the processes involved in their deamination must be very similar.

The 80% retention of configuration observed in the deamination of γ-aminovaleric acid (see below) shows that considerable interaction must occur between the carbonium ion (or a precursor of this ion) and the γ-carboxyl group at the " front " of the carbonium ion centre and accordingly any electrostatic interaction of the α-carboxylate group would have to be directed to the " rear " of the carbonium ion. The two interactions operating simultaneously in the deamination of glutamic acid and glutamine would afford very strong protection for the carbonium ion centre against attack by " outside " entities and this two-fold protection gives a reasonable explanation for the complete absence [6] of the expected intervention [7] by nitrite ion and for the high yield of lactone obtained when nitrous acid reacts with glutamic acid and glutamine under Van Slyke conditions.

The steric course of the cyclisation of the carbonium ion formed in the deamination of

* The difference in the observed optical rotations is probably related to slight variations in experimental procedure between the two sets of experiments and is not considered significant. α-Hydroxyglutaric acid has $[\alpha]_D^{19}$ ±8·65°.[5]

[3] Fuks, *Acta Pharm. Jugoslav.*, 1953, **3**, 35; *Chem. Abs.*, 1955, **49**, 8114.
[4] Balenovic and Cerar, *J.*, 1955, 1631.
[5] Fischer and Moreschi, *Ber.*, 1912, **45**, 2447.
[6] Austin and Howard, following paper.
[7] Austin, *J.*, 1950, 149.

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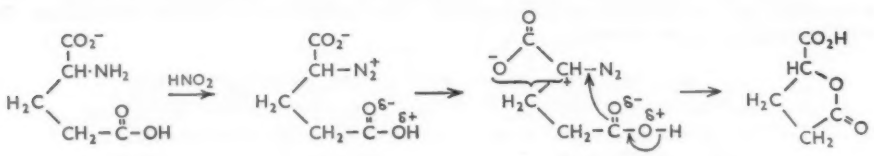
glutamic acid is postulated to involve a spirocyclic transition state, the lactone being formed with retention of configuration at the asymmetric carbon centre:



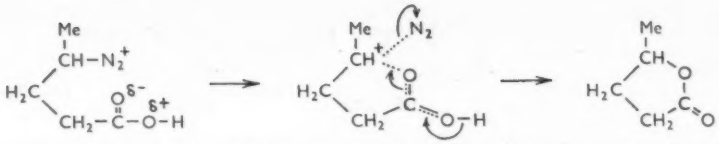
Deamination of (+)-γ-aminovaleric acid, $[\alpha]_D^{22}$ +12° (lit.,[4] +14°), gave unexpected results. The optical activity of the lactone, $[\alpha]_D^{22}$ −13·7° (lit.,[8] −27·75°), and of the hydroxy-acid obtained on hydrolysis, $[\alpha]_D^{22}$ +6° (lit.,[8] +14°), indicated that 80% of the reaction leading to the lactone had proceeded in a manner that retained the optical activity. It thus appeared that " free " carbonium ions are not involved in the formation of the lactone from γ-aminovaleric acid.

Levene and Heller [8] showed that (+)-γ-hydroxyvaleric acid belongs to the L-series and it has been shown in the present investigation and by others [4] that (+)-γ-aminovaleric acid has the same configuration as L-(+)-α-alanine.[9] Therefore, the hydroxy-acid obtained by hydrolysis of (−)-γ-valerolactone must have possessed the same configuration as the parent amine, the amino-compound being converted into the hydroxy-acid with predominant retention of configuration. This overall retention of configuration could have resulted from the γ-valerolactone's being formed from the amine with inversion and hydrolysed with inversion, but this is not so because γ-butyrolactone has been shown kinetically and by tracer studies with ^{18}O to undergo both basic and acidic hydrolysis with acyl–oxygen fission.[10] It is reasonable to assume that the same process would apply to γ-lactones in general. This being the case, hydrolysis of the acyl–oxygen bond of γ-valerolactone would yield the γ-hydroxy-acid with retention of configuration. Therefore the process leading to the lactone must also have occurred with retention of configuration.

This finding contrasts with the deamination of simple amines where, in the absence of an α-carboxyl group, net inversion of configuration was obtained.[1] It also differs from the stereochemical implication that the lactone formed in the solvolysis of γ-bromovaleric acid yielded, on hydrolysis, a hydroxy-acid with inverted configuration.[5,11,12,13] However, in this case it was apparent, from the rate of reaction, that the carboxylate group interacted with the γ-carbon atom in an internal bimolecular process and these bimolecular replacements have been shown to require linear transition states and always to lead to inversion at the centre undergoing replacement.

The S_N1 process for the formation of the lactone from γ-aminovaleric acid having been rejected because of the optical purity of the products, and the S_N2 process having been rejected because of the predominant retention of configuration of the products, the following mechanism is suggested: Electrostatic interaction between the diazonium cation and the γ-carboxyl group is postulated to lead to the formation of a quasi-six-membered ring. As the nitrogen breaks away the six-membered ring collapses to a fully covalent five-membered ring lactone with the oxygen of the γ-carboxyl group entering the site originally occupied by the amino-group by an S_Ni-mechanism: [14]

[8] Levene and Heller, *J. Biol. Chem.*, 1926, **69**, 165.
[9] Brewster, Hughes, Ingold, and Rao, *Nature*, 1950, **166**, 178.
[10] Long and Friedman, *J. Amer. Chem. Soc.*, 1950, **72**, 3692; Long, McDevit, and Dunkle, *J. Phys. Colloid Chem.*, 1951, **55**, 829.
[11] Caldin and Wolfenden, *J.*, 1936, 1239.
[12] Cowdrey, Hughes, Ingold, Masterman, and Scott, *J.*, 1937, 1252.
[13] Ingold, " Structure and Mechanism in Organic Chemistry," Bell and Sons Ltd., London, 1953, 384.
[14] Ref. 13, p. 392.



This mode of electrostatic orientation and formation of lactone would account for both the optical purity of the product and the retention of configuration, for the electrostatic interaction would be much more pronounced on that side of the asymmetric carbon atom leading to retention of configuration. The optical activity indicates that less than 20% of the lactone had been formed by intramolecular S_N2 interaction.

It is no criticism of the above mechanism that electrostatic effects, as depicted above, have been shown not to be important for Walden inversion [15] for no energetically important rate-determining interaction is attributed to the carboxyl group. The incorporation of this " front-side " interaction had been anticipated in the mechanism given on p. 3280 for the steric course of the lactonisation of glutamic acid. Essentially the same steps would apply for the reaction of glutamine. The effect must be strong because it can, in conjunction with the α-carboxylate group, prevent any detectable intervention by nitrite ion and it must be considered as a third factor, additional to the two already established,[2,6] that favours the high yield of lactone in the deamination of glutamic acid and glutamine.

A similar electrostatic orientation would have to be assumed during the deamination of asparagine, but the subsequent formation of a lactone would not be possible here: it would require the collapse of the quasi-five-membered ring to a four-membered ring lactone and this is known to be difficult on both theoretical and experimental grounds.

The possibility that the carboxyl group in γ-aminovaleric acid interacted with the diazonium cation to form a cyclic diazo-ester can be rejected. These compounds have been suggested as intermediates in the thermal decomposition of *N*-nitroso-derivatives [16] and their decomposition was postulated to account for the retention of configuration in the products. These reactions, however, were carried out under different conditions from ours. Moreover, if these diazo-esters were important intermediates in the deamination of γ-carboxy-amines it would be expected that asparagine, which would be able to form the six-membered ring required, would react with nitrous acid to evolve 100% of the nitrogen and this does not happen.

In view of the predominant " front-side " lactonisation observed in the deamination of γ-aminovaleric acid it is relevant that Shoppee *et al.*[17] deaminated saturated steroid equatorial amines in 50% aqueous acetic acid and obtained the corresponding alcohol (100% yield) with retention of configuration. Mills,[18] Streitwieser *et al.*,[19] and Dauben *et al.*[20] have obtained similar results with aminocyclohexanes and aminodecalins. From axial amines Mills and Dauben *et al.* obtained alcohols with predominant inversion together with much olefin. Shoppee *et al.*, however, observed retention of configuration in the deamination of the axial amines they studied (together with much olefin) and this was clearly inconsistent with the conclusions reached by the other workers that deamination of this type of compound is conformationally specific. Since there was no configuration-holding group present Shoppee *et al.* considered that carbonium ions were not formed and concluded that the reaction involved the interaction of water with the diazonium cation in a pyramidal transition state; but an immediate objection to this explanation became apparent when it was shown that the olefin formed conformed to the Saytzeff rule whereas elimination from the diazonium cation should have been governed by the Hofmann rule.

[15] Read and Walker, *J.*, 1934, 308.
[16] White, *J. Amer. Chem. Soc.*, 1955, **77**, 6014.
[17] Shoppee, Evans, and Summers, *J.*, 1957, 97.
[18] Mills, *J.*, 1953, 260.
[19] Streitwieser and Coverdale, *J. Amer. Chem. Soc.*, 1959, **81**, 4275.
[20] Dauben, Tweit, and Mannerskantz, *J. Amer. Chem. Soc.*, 1954, **76**, 4420.

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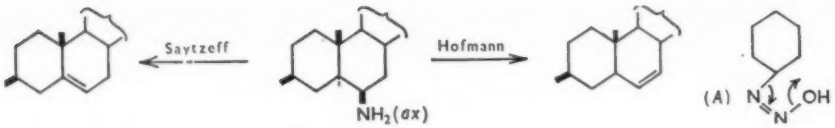

Deamination of equatorial amines affords no inverted products and no olefin, hence it appears that free carbonium ions are not formed in the reaction. This is plausible because flattening of part of an alicyclic ring system is not easy and the formation of carbonium ions has been shown to require at least partial planarity.[21,22] The products of reaction have accordingly to be derived from something other than a carbonium ion. Bimolecular replacement is difficult in these systems because the other atoms in the ring system sterically hinder the formation of a linear transition state, and bimolecular elimination is difficult because a *trans*-planar transition state is difficult to realise. Another reaction path is brought into play and it is suggested that the diazohydroxide undergoes decomposition by an S_Ni mechanism (cf. *A*). S_Ni reactions preserve the essential features of unimolecular reactions [12,13] with the special feature that they result in retention of configuration in the products. Although Bartlett [23] has suggested a similar mechanism for the deamination of 1-apocamphylamine it is clear that he does not consider the process to be similar to the unimolecular ionisation process.

Deamination of axial amines always leads to a considerable proportion of olefin—it is usually the major product and in one of Shoppee's examples was the sole product in quantitative yield. The explanation for this is that the *trans*-planar transition state is easily achieved with axial amines as Mills [18] pointed out. Notwithstanding, the proportion of the olefin is always extremely high and this poses the question whether (*a*) olefin-formation is very easy or (*b*) substitution is very difficult. The question must be asked in the absolute sense as well as in the relative sense.

It seems that (*b*) contains the answer since the conditions obtaining in deamination (aqueous acetic acid) are not normally conducive to high yields of olefin. Bimolecular replacement would be difficult because extensive compression would arise in the formation of the linear transition state where four quasi-axially disposed groups would be on one side of the ring and three on the other, which is untenable in terms of conformational energy. Unimolecular replacement would also be difficult because flattening of part of a ring system is not easy and, as already noted, at least partial planarity is required for the formation of carbon ions. It is, therefore, clear that in these cases olefin formation, even in mild conditions of aqueous acetic acid, will not be in serious competition with substitution.

With the axial amino-derivatives of the smaller ring systems of cyclohexane and the decalins the experimental results require the assumption that distortion and buckling of the rings with concomitant conformational eclipsing of the hydrogen atoms is energetically realisable in order to account for an amount of equatorial product in excess of the axial product (9 : 1). It is rational to assume that buckling and distortion of the preferred conformation will extend from atom to atom over the whole molecule. If the ring system is extended (as in Shoppee's examples) it is only to be expected that the buckling and conformational eclipsing that must occur in the formation of the linear (or near-linear) S_N2 transition state at any part of the molecule will involve the spatial adjustments of many more atoms, and the energy required for that particular reaction would be correspondingly increased. Alternative reaction paths such as substitution by the S_Ni mechanism (cf. *B*) and elimination could then predominate.

This postulate that the diazohydroxide leads directly to the products gives a consistent explanation for Shoppee's observation that elimination is Saytzeff-controlled—the olefin

[21] Bartlett and Knox, *J. Amer. Chem. Soc.*, 1939, **61**, 3184.
[22] Doering, Levitz, Sayigh, Sprecher, and Whelan, *J. Amer. Chem. Soc.*, 1953, **75**, 1008.
[23] Bartlett in Gilman's "Organic Chemistry," Wiley and Sons, New York, 1953, Vol. III, p. 45.

is formed by fragmentation of the non-polar diazohydroxide and is not derived from the polar diazonium cation (cf. *C*).

Experimental

Deamination of L-(+)-*Glutamic Acid.*—Glutamic acid (0·7 g.), $[\alpha]_D^{19}$ +29·6° in 5% HCl, was added to saturated aqueous sodium nitrite (2 c.c.); then glacial acetic acid (0·5 c.c.) was added After 10 min. the solution was evaporated to dryness under a vacuum. The residue was hydrolysed for 1 hr. with 2N-sodium hydroxide (2 c.c.), and the optical rotation of the alkaline solution of sodium α-hydroxyglutarate was measured ($[\alpha]_D^{21}$ −9·2° ± 0·4°).

Deamination of L-(+)-*Glutamine.*—In the same conditions glutamine (0·3 g.), $[\alpha]_D^{21}$ +6·75° (in water), was converted into the hydroxy-glutaric acid and the alkaline solution gave $[\alpha]_D^{21}$ −7·5° ± 0·4°.

Deamination of (+)-γ-*Aminovaleric Acid.*—(+)-γ-Aminovaleric acid (1 g.), $[\alpha]_D^{22}$ +12°, was dissolved in 2N-acetic acid (5 c.c.), and 0·4N-aqueous sodium nitrite (25 c.c.) was added during 1 hr. This slow addition minimised the formation of nitro-compounds. The solution was extracted with ether (6 × 30 c.c.) and after removal of the ether (in a vacuum) the lactone residue was dissolved in water (10 c.c.) and shaken with charcoal. After filtration the optical rotation was measured in a 2-dm. tube and the lactone concentration was then determined colorimetrically:[6] $[\alpha]_D^{22}$ −13·8° (c = 0·85).

A sample of the lactone solution was hydrolysed with an excess of 0·2N-barium hydroxide and the optical rotation measured: $[\alpha]_D^{22}$ +6°. On acidification the solution became lævorotatory as the hydroxy-acid lactonised.

The partition coefficient for the distribution of γ-valerolactone between ether and water was found to be K (ether/water) = 0·525 at 20°. Experiments showed that less than 2% of the free hydroxy-acid was extracted by ether in 3—4 hr. from a neutral aqueous solution of γ-hydroxyvaleric acid.

Optical Resolution of γ-*Aminovaleric Acid.*—γ-Aminovaleric acid, prepared from lævulic acid, was resolved through the benzoyl derivative with quinine (cf. Fischer and Groh [24]): it had $[\alpha]_D^{22}$ +12° (lit.,[4] $[\alpha]_D^{22}$ +13·9°).

Preparation of (+)-β-*Aminobutyric Acid.*—Crotonic acid was treated with concentrated aqueous ammonia at 140°. The amino-acid was esterified, purified by distillation, and resolved with β-camphorsulphonic acid.[25] (The optically pure isomers were not prepared. It was sufficient for our purpose to have one isomer in sufficient excess.) The acid obtained on hydrolysis, $[\alpha]_D^{19}$ +5° in water (lit.,[25] $[\alpha]_D^{25}$ +35·3°), gave β-benzamidobutyric acid, m. p. 152°, $[\alpha]_D^{19}$ +6° in 2N-sodium hydroxide.

Conversion of Ethyl (+)-β-*Amino*-β-*methylbutyrate into Benzoyl*-α-*alanine* (*Barbier–Wieland*).—Ethyl β-amino-β-methylbutyrate was converted by conventional methods into 3-amino-1,1-diphenylbutan-1-ol, m. p. 154—155° (from light petroleum) (Found: C, 79·8; H, 7·9; N, 5·65. Calc. for $C_{16}H_{19}NO$: C, 79·5; H, 7·9; N, 5·8%), whose benzoyl derivative (prepared by benzoyl chloride–pyridine), m. p. 164° (Found: C, 79·65; H, 6·45; N, 4·35. Calc. for $C_{23}H_{23}NO_2$: C, 80·0; H, 6·66; N, 4·1%) (2 g.) was heated for 30 hr. with chloroform and iodine; the glassy residue obtained after removal of iodine was oxidised with potassium permanganate in acetone, giving benzoyl-α-alanine, m. p. 159°, $[\alpha]_D^{18}$ +6·8° in 2N-sodium hydroxide (Found: C, 61·8; H, 5·65; N, 7·45. Calc. for $C_{10}H_{11}NO_3$: C, 62·2; H, 5·7; N, 7·25%).

Conversion of (−)-γ-*Aminovaleric Acid into* β-*Benzamidobutyric Acid* (*Barbier–Wieland*).—The combined filtrates from the optical resolution of γ-aminovaleric acid (see above) afforded (−)-γ-benzamidovaleric acid, $[\alpha]_D^{20}$ +16° (lit.,[24] +21·9°). This was hydrolysed with 20%

[24] Fischer and Groh, *Annalen*, 1911, **383**, 370.
[25] Fischer and Scheibler, *Annalen*, 1911, **383**, 344.

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hydrochloric acid and esterified with methanolic hydrogen chloride. The ester was then converted, via the tertiary alcohol and the derived olefin, into β-benzamidobutyric acid, m. p. 152°, $[\alpha]_D^{19}$ −6·65° in 2N-sodium hydroxide (Found: C, 63·6; H, 6·35; N, 6·7. Calc. for $C_{11}H_{13}NO_3$: C, 63·6; H, 6·3; N, 6·8%).

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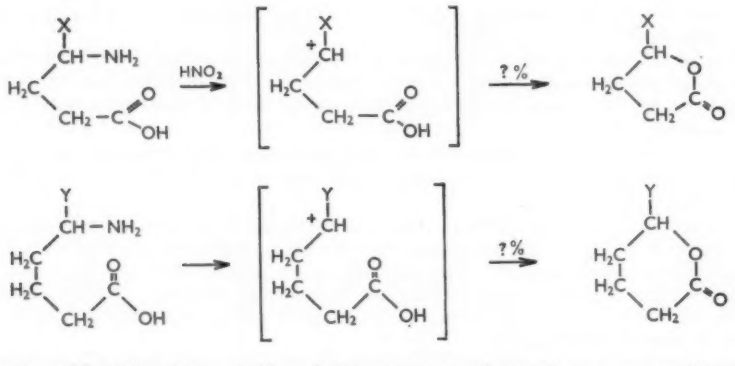
643. *The Deamination, by Nitrous Acid, of Amino-acids structurally Related to Glutamic Acid: γ-Aminobutyric, γ-Aminovaleric, α-Aminoadipic, and δ-Aminovaleric Acid, and Isoglutamine.*

By A. T. AUSTIN and J. HOWARD.

The amount of lactone formed in the deamination of glutamic acid by nitrous acid decreases to one-third when the carboxyl group in the α-position to the amino-group is replaced by H or Me. This is attributed to a configuration-holding effect of the α-carboxylate group that minimises intermolecular attack on the intermediate carbonium ion. With amines that give, on deamination, five-membered ring lactones, the yield of lactone is nine times greater than from those amines that give six-membered ring lactones.

THE evolution of two mol. of nitrogen instead of the one expected when glutamine reacts with nitrous acid (Van Slyke determination) has been shown to be related to the formation of a lactone which was postulated to arise because the carbonium ion (formed by the action of nitrous acid on the α-amino-group) underwent intramolecular cyclisation with the oxygen of the amido-group.[1] The same lactone is formed, to the same extent (93%), in the reaction



of glutamic acid with nitrous acid and the sequence of reactions was considered to be essentially the same for both glutamine and glutamic acid.

The compounds noted in the title were subjected to deamination by nitrous acid for the purpose of establishing whether the extent of the lactonisation is influenced by the presence of the carboxyl group in the α-position to the amino-group, and the size of the lactone ring. These items may be depicted in the generalised form as annexed, where X = CO_2H, H, Me, or $CO{\cdot}NH_2$, and Y = CO_2H or H.

RESULTS

Deamination of γ-Aminobutyric Acid.—Fig. 1 shows the rate of disappearance of γ-aminobutyric acid from aqueous nitrous acid solutions of this compound and the rate of formation of

[1] Austin and Howard, *J.*, preceding paper.

lactone in the same solution. From the respective gradients it is seen that the initial rate of deamination is approximately three times that for the formation of the lactone. The broken line shows the calculated amount of lactone that would have been formed if the deamination led directly to γ-hydroxybutyric acid which then gave the lactone.

Deamination of γ-Aminovaleric Acid.—Similar plots for this acid are shown in Fig. 2. The gradients show that the initial rate of deamination of γ-aminovaleric acid is four times the initial rate of formation of γ-valerolactone.

Deamination of Isoglutamine, α-Aminoadipic Acid, and δ-Aminovaleric Acid.—Kinetic measurements were not carried out with these compounds. Instead solutions 0·02M with respect to the amino-compound and 0·04M in nitrous acid were prepared (as for the kinetic determinations) and the amount of deamination and lactone formation measured after ½ hr.

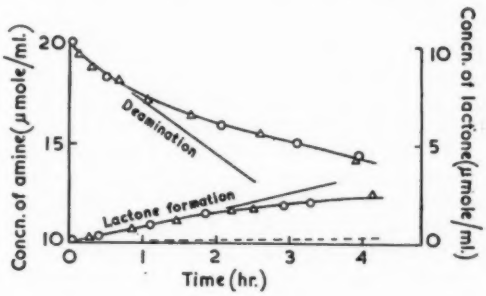


FIG. 1. *Reaction–time curves for* [γ-Aminobutyric Acid] = 0·02M + [HNO_2] = 0·04M *in aqueous solution at* 25·0°, pH = 2·8, *and* p_{NO} = 1 atm.

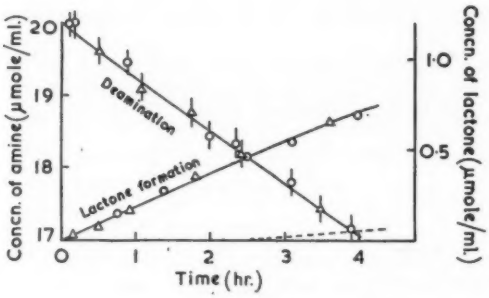


FIG. 2. *Reaction–time curves for* [γ-Aminovaleric acid] = 0·02M + [HNO_2] = 0·04M *in aqueous solution at* 25·0°, pH = 2·7, p_{NO} = 1 atm.

for the solution containing isoglutamine and after 2—3 hr. for solutions containing α-aminoadipic and δ-aminovaleric acid. 46% of the deaminated isoglutamine appeared as lactone; the corresponding figures for α-aminoadipic and δ-aminovaleric acid were 10% and 3% respectively.

Rate of Lactonisation of Hydroxy-acids.—Rates of lactonisation were determined at 25·0° in aqueous solution as follows: γ-hydroxybutyric, $k = 7{\cdot}2 \times 10^{-4}$; γ-hydroxyvaleric, $2{\cdot}8 \times 10^{-3}$; δ-hydroxyvaleric acid, $4{\cdot}5 \times 10^{-3}$ mole^{-1} l. sec.$^{-1}$.

Discussion

As the rate of lactonisation of the hydroxy-acid is unable to account for any but a negligible amount of lactone one may assume that all the lactone formed in the initial stages is derived directly from the intramolecular cyclisation of the carbonium ion with the γ- or δ-carboxyl group. The following Table is drawn up from the ratio, initial rate of deamination/initial rate of lactone formation, to obtain the percentages of lactone formed in the deamination of γ-amino-butyric and -valeric acid; the entries for the last three compounds in the Table record the percentage of lactone obtained by direct measurement.

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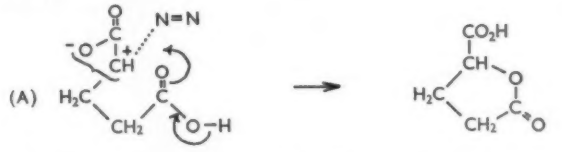
Effect of (a) *changing the group α to the amino-group and* (b) *size of lactone ring, on percentage of deamination leading to lactone.*

Acid	"α"-Group	Ring size of lactone	Lactone (%)
Glutamic	CO_2H	5	93 [1]
γ-Aminobutyric	H	5	33
γ-Aminovaleric	Me	5	25
Isoglutamine	$CO{\cdot}NH_2$	5	46
α-Aminoadipic	CO_2H	6	10
δ-Aminovaleric	H	6	3·5

(a) *Effect of changing the Group α to the Amino-group.*—When optically active halogeno-acids were solvolysed under unimolecular conditions retention of configuration at the asymmetric centre was observed and Hughes and Ingold [2] attributed the retention to the carboxylate group's holding a pyramidal transition state until the new group entered the position vacated by the outgoing group. Hughes, Ingold, and their collaborators [3] observed retention of configuration at the asymmetric centre also when optically active amino-acids were deaminated with nitrous acid, and a mechanistic interpretation similar to that given for the halogeno-acids was invoked.

In the present investigation a sharp drop in the yield of lactone (93 to 33%) was observed when the α-carboxyl group in glutamic acid was replaced by hydrogen, and a similar drop (10% to 3·5%) from α-aminoadipic to δ-aminovaleric acid. These results suggest that the α-carboxyl group acts in the configuration-holding manner discussed in the preceding paper and so impedes intermolecular interaction at the carbonium ion site. It would then be expected that the γ-carboxyl group (or any other nucleophilic entity) would be repelled if it approached the rear of the carbonium ion. For example, interaction of glutamic acid would be restricted to the site vacated by the N_2^+ group in an S_Ni-type reaction (cf. A).

The carbonium ion would not be so effectively protected from rear attack if the α-carboxylate group were replaced by H, Me, or $CO{\cdot}NH_2$; other reactions (solvent, NO_2^- intervention) could compete with interaction of the γ-carboxyl group and the yield of lactone would be expected to fall.



This interpretation implies that the "holding" or "protecting" effect of the α-carboxylate group, invoked by the Hughes–Ingold school to explain the stereochemistry, also exerts a decisive influence on the nature of the reaction, and this, second, aspect is important in minimising "extraneous" reactions during the deamination of glutamine and of glutamic acid where the lactone yield is 93% and the evolved gas is pure nitrogen.

The interpretation is also consistent with the observation [4] that triethyl γ-glutamyl-glutamate evolved 59% of the total nitrogen in the Van Slyke determination, whereas γ-glutamylglutamic acid yielded two mol. of lactone and ~100% of the total nitrogen * under the same conditions.[5] Esterification of the α-carboxyl group reduced the amount of cyclisation and the yield of nitrogen.

* As with glutamine and γ-*N*-methylglutamine the "extra" gas is derived from the nitrosative breaking of the CO·NH bond of the original γ-amide group after this has been modified by intramolecular interaction with the α-carbonium ion.

[1] Ingold, "Structure and Mechanism in Organic Chemistry," Bell and Son, London, 1953, p. 381.
[2] Brewster, Hiron, Hughes, Ingold, and Rao, *Nature*, 1950, **166**, 179.
[3] Boothe, Mowat, Hutchings, Angier, Waller, Stokstad, Semb, Gazzola, and Subba Row, *J. Amer. Chem. Soc.*, 1948, **70**, 1099.
[4] Sachs and Brand, *J. Amer. Chem. Soc.*, 1954, **76**, 3601.

(b) *Effect of Ring-size of the Lactone.*—Although glutamic acid gave a 93% yield of the five-membered ring lactone, γ-carboxy-γ-butyrolactone, the next higher homologue, α-aminoadipic acid, gave only 10% of the six-membered ring lactone, δ-carboxy-δ-valerolactone. There was a similar nine-fold decrease in the amount of lactone when passing from γ-aminobutyric (giving a five-membered ring in γ-butyrolactone) to δ-aminovaleric acid (giving a six-membered ring in δ-valerolactone).

As it was not possible to detect any lactone after the deamination of aspartic acid [1] (which would have given a four-membered ring lactone) one can conclude that five-membered rings are much more easily formed in the deamination. One could cite many examples of other reactions where the formation of five-membered rings is preferred to that of six-membered rings and it is relevant van Tamelen and Shamma [6] found interaction of iodine with βγ- and γδ-unsaturated acids to give preferentially the five-membered iodo-lactones. The ease of formation of five-membered ring lactones is a general phenomenon and is understandable in terms of ring-angle strain and non-bonded interaction of the substituents; it is undoubtedly important in determining the high yield of lactone from glutamic acid and glutamine and, together with the " protecting " effect of the α-carboxyl group, underlies the marked anomaly when glutamine is determined in the Van Slyke procedure.

The ability of remote parts of a molecule to approach each other (by rotation) and in so doing to modify the chemistry when one of the parts is chemically attacked underlies the anomalous behaviour of a number of organic reactions.[7] It has been invoked [8] to explain Birkinshaw's observation that palitantin readily takes up one atom of iodine from ethanolic iodine to form a mono-iodo-compound in 80% yield.[9] The cyclic intermediate postulated here to account for the anomalous behaviour of glutamine is also involved in the selective splitting of tyrosyl [10] and tryptophyl [11] peptides and in the explanation [10] for the unexpected degradation of oxytocin by bromine water.[12]

The anomalous result created is most pronounced when the internal interactions can reach the reaction site by formation of five- or six-membered rings and the term " chelate interaction " is suggested to denote these modifications in chemical behaviour caused by intervention of a part of the molecule normally remote from the site of reaction.

Experimental

γ-Aminobutyric Acid.—γ-Chlorobutyryl chloride [13] was converted into ethyl chlorobutyrate by addition to absolute ethanol, and the fraction of b. p. 186—188° was used to prepare the γ-phthalimido-ester by Sheehan and Bolhofer's method.[14] The phthalimido-group was removed by hot 50% sulphuric acid, and the amino-acid obtained on neutralisation with barium carbonate crystallised from water on addition of ethanol; it had m. p. 199—201° (decomp.) (Found: C, 46·5; H, 8·5; N, 13·4; Van Slyke determination, 99·2. Calc. for $C_4H_9NO_2$: C, 46·6; H, 8·7; N, 13·4%).

γ-Aminovaleric Acid.—Lævulic acid was converted into the phenylhydrazone which was reduced to γ-aminovaleric acid by Fischer and Groh's method.[15] Crystallised twice from water by addition of ethanol, it had m. p. 162° (lit.,[9] 162°). A Van Slyke determination gave 100·0% of nitrogen.

[6] Van Tamelen and Shamma, *J. Amer. Chem. Soc.*, 1954, **76**, 2315.
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[13] Loftfield, *J. Amer. Chem. Soc.*, 1951, **73**, 1365.
[14] Sheehan and Bolhofer, *J. Amer. Chem. Soc.*, 1950, **72**, 2786.
[15] Fischer and Groh, *Annalen*, 1911, **383**, 370.

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α-Aminoadipic Acid.—The method of Waalkes, Fones, and White,[16] starting with adipic acid, was modified by using dimethylformamide as the solvent for the reaction between the α-bromoadipic ester and potassium phthalimide. The phthalimido-group was removed by hydrochloric acid,[17] and the free amino-acid obtained by passing the hydrochloride through Zeo-Karb 216 (20—60 mesh) [1] (Found: C, 44·5; H, 6·9; N, 8·9; Van Slyke determination, 98. Calc. for $C_6H_{11}NO_4$: C, 44·75; H, 6·8; N, 8·7%).

δ-Aminovaleric Acid.—Cyclopentanone [18] was converted into the oxime which was heated with 30N-sulphuric acid.[19] The α-piperidone was hydrolysed with 2N-sulphuric acid and after neutralisation (barium carbonate) was purified by passage through Zeo-Karb 216 (20—60 mesh).[1] Recrystallisation from water by addition of ethanol (twice) gave an acid, m. p. 158° (lit.,[20] 157—158°) (Found: C, 50·45; H, 9·35; N, 11·6; Van Slyke determination, 95. Calc. for $C_5H_{11}NO_2$: C, 51·2; H, 9·4; N, 12·0%).

δ-Valerolactone.—This was prepared by Schniepp and Geller's method [21] from pentane-1,5-diol. Saponification showed 99% purity.

γ-Butyrolactone and γ-Valerolactone.—Commercial material was purified by distillation. Fractions, b. p. 203—204° and 207°, respectively, were used.

Estimation of Lactones.—These lactones were used to prepare the calibration between optical density and lactone concentration in colorimetric estimations of the lactones formed in the deaminations: the ferric–hydroxamic acid colour complex was used with the procedure already described.[1] γ-Carboxy-γ-butyrolactone, γ-butyrolactone, and γ-valerolactone gave the same optical density for the same concentration of lactone. δ-Valerolactone required 20 min. for quantitative reaction with the hydroxylamine and a separate calibration chart as the calibration was different from that for the five-membered ring lactones. As the other three lactones gave identical calibration charts it was assumed that the calibration chart for δ-carboxy-δ-valerolactone would be the same as for δ-valerolactone and the one chart was used for estimating these two lactones.

Estimation of Amino-acids.—(a) *γ-Aminobutyric acid.* This acid was estimated by Sörensen's formol titration, the copper complex and the ninhydrin method previously [1] used being restricted to α-amino-acids. The determinations were readily reproducible but in our hands the first pink colour of phenolphthalein in the titrations always corresponded to only 92% reaction. Simultaneous potentiometric titrations also gave the end-points at 92% reaction and pH 8·5. At pH 9, the pH usually quoted for the end-point, the titrations corresponded to 100% reaction but at this pH the maximum gradient in the potentiometric titration had been passed and the colour of the phenolphthalein was so intense that comparison with a colour standard was impossible. Identical behaviour was obtained when several different samples of carefully purified glycine were tested. As, however, the end-point to the first pink of phenolphthalein was sharp and reproducible the method was used to estimate γ-aminobutyric acid and the concentration so obtained was " corrected " by use of the factor 100/92.

(b) *γ-Aminovaleric acid.* The Sörensen formol titration gave unsatisfactory results, and potentiometric titration was also unsatisfactory as the $\Delta pH/\Delta V$ gradient was quite small at the end-point. The acid was therefore determined by the Van Slyke procedure. During the runs samples were removed from the reaction vessel and plunged into 0·01N-sodium hydroxide to stop the reaction. The amino-nitrogen was then determined. The results were reproducible to ±1%.

(c) *α-Aminoadipic and δ-aminovaleric acid.* These were most conveniently determined by the Van Slyke procedure. Although there is some uncertainty surrounding the method the results are reproducible when the stated conditions are adhered to and the results obtained had the accuracy required. The Van Slyke apparatus was the manometric type supplied by Messrs. Gallenkamp & Co., Ltd., London.

Determination of Rate Constants for the Lactonisation of γ-Hydroxybutyric, γ-Hydroxyvaleric, and δ-Hydroxyvaleric Acid.—These were determined as described for γ-hydroxyglutaric acid.[1] The results were calculated on the basis of initial rates and the determinations were made over

[16] Waalkes, Fones, and White, *J. Amer. Chem. Soc.*, 1950, **72**, 5760.
[17] Gaudry, *Canad. J. Res.*, 1949, **27**, *B*, 21.
[18] Vogel, " Textbook of Practical Organic Chemistry," Longmans, Green & Co., London, 1956, 3rd edn., p. 340.
[19] Fox, Dunn, and Stoddard, *J. Org. Chem.*, 1941, **6**, 410.
[20] Wallach, *Annalen*, 1900, **312**, 180.
[21] Schniepp and Geller, *J. Amer. Chem. Soc.*, 1947, **69**, 1545.

the pH range 1·3—2·3. The rates were all of the same order of magnitude and it was assumed that for α-hydroxyadipic acid it would also be of the same order.

Run Procedure.—The experimental procedure was as described for the kinetic investigations with glutamine and glutamic acid.[1] Samples were withdrawn at timed intervals and run into the appropriate solutions for the estimation of the unchanged amino-compound, and the lactone was determined by the method already described.[1]

SCHOOL OF CHEMISTRY, UNIVERSITY OF LEEDS, LEEDS, 2. [*Received, January 16th*, 1961.]

644. *The Crystal Structure of Anhydrous Copper(II) Formate.*

By G. A. BARCLAY and C. H. L. KENNARD.

The crystal structure of royal-blue anhydrous copper(II) formate has been determined by *X*-ray diffraction techniques involving three-dimensional Fourier syntheses. There are eight molecules in the orthorhombic unit cell (space group *Pbca*) with dimensions $a = 14{\cdot}195 \pm 0{\cdot}005$, $b = 8{\cdot}955 \pm 0{\cdot}005$, and $c = 6{\cdot}218 \pm 0{\cdot}005$ Å. There are no discrete molecules in the crystal; it consists of a three-dimensional array or copper atoms joined together by formate groups in an "*anti-syn*" bridging arrangement. Each copper atom has a distorted tetragonal-pyramidal co-ordination of four oxygen atoms, at a distance of 1·95 Å in a plane containing the copper atom, and a fifth oxygen atom at 2·40 Å along a line which makes an angle of 31° with the normal to this plane.

THREE different anhydrous copper(II) formates have been identified by measurements of their magnetic susceptibilities and *X*-ray diffraction powder patterns.[1] Two of these, which are formed as powders by the dehydration of the di- and tetra-hydrates, exhibit unusual magnetic properties ($\mu = 1{\cdot}75$ and 1·61 B.M. respectively). The third is obtained as well-formed royal-blue crystals from concentrated formic acid solution kept at 100° for several hours. The magnetic moment of this modification shows no unusual features ($\mu = 1{\cdot}90$ B.M.). Because of the interest in the stereochemistry of these and related copper(II) salts of carboxylic acids,[2] the crystal structure of royal-blue anhydrous copper(II) formate was determined.

EXPERIMENTAL

The orthorhombic crystals are thin plates lying on their 010 faces. Accurate cell dimensions were obtained by using a Hägg focusing powder camera. The systematically absent reflections (0*kl*, with $k = 2n + 1$; *h*0*l*, with $l = 2n + 1$; *hk*0, with $h = 2n + 1$) indicate the space group *Pbca* unambiguously. Intensities were estimated visually from equi-inclination Weissenberg photographs by the multiple-film technique. They were corrected for the Lorentz and polarisation factors; no allowance was made for absorption or extinction. The intensities were placed on a common arbitrary scale by internal correlation and eventually the observed structure amplitudes were scaled to the calculated values.

Crystal Data: $Cu(H{\cdot}COO)_2$; $M = 153{\cdot}61$; orthorhombic; $a = 14{\cdot}195 \pm 0{\cdot}005$, $b = 8{\cdot}955 \pm 0{\cdot}005$, $c = 6{\cdot}218 \pm 0{\cdot}005$ Å; $U = 709{\cdot}41$ Å^3; $D_m = 2{\cdot}58 \pm 0{\cdot}01$ g. cm.$^{-3}$ (by flotation); $Z = 8$; $D_c = 2{\cdot}580$ g. cm.$^{-3}$; $F(000) = 600$; space group — *Pbca* (D_{2h}^{15}, No. 61). Radiation copper, unfiltered; single-crystal rotation, oscillation and equi-inclination Weissenberg photographs. Data for structure analysis from *hk*0 ⟶ *hk*4, *h*0*l* ⟶ *h*4*l*, 0*kl* ⟶ 4*kl*.

TABLE 1. *Atomic parameters.*

Atom	*x/a*	*y/b*	*z/c*	σ (Å)	Atom	*x/a*	*y/b*	*z/c*	σ (Å)
Cu	0·1152	0·0588	0·0065	0·002	O(4)	0·1493	−0·1207	−0·1459	0·010
O(1)	0·0893	0·2427	0·1621	0·009	C(1)	0·0184	0·3226	0·1613	0·010
O(2)	0·2223	0·0262	0·1950	0·009	C(2)	0·2778	0·1353	0·2336	0·011
O(3)	0·0067	0·0781	−0·1902	0·008					

[1] Martin and Waterman, *J.*, 1959, 1359.
[2] Martin and Waterman, *J.*, 1957, 2545.

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TABLE 2. *Calculated structure factors and observed structure amplitudes.*
(Scale: ½ absolute values.)

h	F_c	$\|F_o\|$	h	F_c	$\|F_o\|$	h	F_c	$\|F_o\|$	h	F_c	$\|F_o\|$	h	F_c	$\|F_o\|$	h	F_c	$\|F_o\|$
	h,0,0			h,1,3			h,2,3			h,3,3			h,4,5			h,6,1	
2	19	18	1	31	29	1	−35	29	1	16	18	1	−28	26	0	7	8
4	−51	45	2	−3	5	2	−15	16	3	−26	26	3	−26	25	1	−38	33
6	−19	22	3	−28	29	3	−47	38	4	−7	9	4	10	12	3	−35	32
8	85	74	4	−6	8	4	13	13	5	−39	35	5	11	14	5	22	20
10	46	43	5	−66	47	5	33	29	6	13	16	7	26	27	6	13	14
12	−20	23	7	11	14	6	−10	12	7	16	16	10	−4	14	7	33	30
14	−5	10	9	32	31	7	26	26	8	−11	11	11	−25	27	9	−9	9
18	22	20	13	−40	35	8	−7	8	9	4	7				11	−21	22
	h,0,2		15	−5	6	9	−16	18	10	5	6		h,4,7		15	13	12
0	11	11				11	−19	22	12	−6	6	0	−7	9			
1	−17	16		h,1,4		15	13	14	13	−14	15	1	−12	14		h,6,2	
2	15	17	1	8	9							3	−18	20	0	−27	27
3	−6	4	2	−18	18		h,2,4			h,3,4		5	8	12	2	9	10
4	−107	67	3	−4	6	0	52	39	1	−22	21				3	11	11
5	−33	35	5	−7	9	2	10	13	2	−56	48				4	23	26
6	−25	26	6	24	23	3	−25	25	3	−12	15		h,5,0		6	13	14
7	19	21	10	−7	9	4	−36	34	4	−13	15	2	−90	70	7	−11	12
8	37	35	14	10	11	6	−16	17	6	42	37	4	−7	9	8	−17	18
9	15	16				8	26	26	8	13	15	6	43	39	9	−11	13
10	16	19		h,1,5		10	19	20	9	−13	13	8	39	37	10	−6	9
11	−15	14	1	38	35	12	−12	14	10	−20	19	10	−35	33	12	19	21
12	−32	31	2	−13	13	13	−10	11	11	−13	14	12	−11	17	14	10	12
13	−7	8	3	−18	20	14	−12	14	12	−16	18	16	16	16			
14	−36	33	5	−22	22				14	8	10					h,6,3	
16	21	20	6	12	10		h,2,5						h,5,1		1	−10	14
			7	11	12	1	−26	24		h,3,5		1	−23	23	3	−29	28
	h,0,4		8	−8	7	3	−19	19	1	18	19	2	−14	16	5	9	14
0	45	41	9	37	30	4	−11	11	3	−12	12	3	7	8	7	24	24
1	10	12	12	−4	5	5	9	10	5	−5	8	4	12	13	11	−24	25
2	−6	6	13	−14	16	7	22	21	8	12	11	5	9	10			
3	−12	13				10	−11	9	9	20	16	7	−17	17		h,6,4	
4	−35	37		h,1,6		11	−18	18	13	−4	6	9	−10	10	0	−17	20
5	22	22										12	10	10	2	−7	9
6	−25	24	2	−17	18		h,2,6			h,3,6					4	15	17
8	35	33	4	−10	8	0	20	18	2	−19	20		h,5,2		8	−16	18
9	−9	8	8	12	9	1	−22	21	3	6	7				9	9	11
10	23	22	10	−10	10	4	−16	16	5	10	9	2	−43	40	10	−8	7
12	−29	28				8	18	20	6	16	16	3	10	12	11	8	8
14	−17	17		h,1,7		10	6	8	7	6	6	4	−18	20	12	10	11
15	10	9	1	16	14				8	10	10	5	16	19			
			2	−8	7		h,2,7		10	−20	19	6	51	44		h,6,5	
	h,0,6		3	−19	16	3	−14	13		h,3,7		7	22	23	1	−18	17
0	54	47	5	−23	19	4	12	12	1	7	8	8	7	10	3	−16	17
1	−18	14	7	8	7	5	6	8	5	−9	9	10	−21	23	4	10	9
2	15	16	8	10	8	6	5	7				12	−25	23			
4	−31	28				7	15	15		h,4,0		14	21	21		h,6,6	
6	−5	7		h,2,0					4	−9	12	15	5	5	0	−18	16
7	9	7	0	72	41		h,3,0		6	−35	36				4	16	13
8	28	27	2	−21	22	2	−40	46	8	−7	12		h,5,3				
10	17	17	4	−28	29	4	−10	12	10	15	16	3	16	17		h,7,0	
			6	−5	5	6	42	39	14	−8	12	5	18	21	2	−29	31
	h,1,0		8	50	48	8	20	22				7	17	17	4	10	10
2	−44	40	10	18	21	10	−44	44		h,4,1		9	−11	12	6	11	11
4	−51	41	12	−30	30	12	−27	27	1	−51	46	11	5	8	10	−27	27
6	18	23	14	−10	15	14	24	24	2	15	17	13	10	10			
8	23	25	16	14	17	16	20	21	3	−55	48					h,7,1	
10	−12	15							5	23	28		h,5,4		1	−32	30
12	−29	27		h,2,1			h,3,1		6	7	11	1	−8	10	2	8	9
18	−7	7	0	−19	19	1	31	28	7	48	56	2	−33	33	3	15	15
			1	−32	29	2	−22	22	9	−15	17	3	−7	9	5	29	28
	h,1,1		2	57	45	3	−9	9	11	−43	36	4	−5	9	7	−10	14
1	81	53	3	−39	39	4	19	21	12	8	12	6	22	24	9	−29	29
2	9	12	4	26	27	5	−17	19	15	21	23	7	−20	19	12	−4	6
3	−58	47	5	11	11	6	−17	18	16	5	5	8	17	17			
4	4	5	6	18	21	7	4	6		h,4,2		10	−29	29		h,7,2	
5	−59	46	7	48	41	8	5	7	0	9	10	12	−14	16	2	−20	20
6	−6	7	8	6	9	9	30	32	1	−26	27	13	5	5	3	−10	10
7	28	26	10	15	17	10	−19	18	3	−13	15				4	−13	14
8	23	24	11	−33	32	12	9	9	5	6	9		h,5,5		5	−14	14
9	55	43	12	9	9	13	−15	19	6	10	12	1	−11	11	6	24	26
11	−7	9	15	22	23	14	−10	9	7	6	11				8	7	9
13	−27	27	16	11	13	17	11	12	8	9	13		h,5,6		9	−9	10
16	7	8	17	5	6				15	−9	11	2	−30	24	12	−13	15
17	19	21					h,4,3					3	10	9			
				h,2,2		0	−11	13				4	−8	7		h,7,3	
	h, 1,2		0	51	37	1	−32	31							1	−17	19
1	−34	31	2	19	18	2	−8	13					h,5,7		3	28	25
2	−25	25	3	27	27	3	−48	45				1	−6	5	5	28	29
3	13	15	4	−71	50	5	32	35				3	7	5	7	−7	9
4	10	12	6	−23	25	7	47	50							9	−16	18
5	15	16	8	30	31	8	−8	9					h,6,0		11	9	11
6	22	23	10	19	21	11	−23	24									
8	10	13	12	−17	21	15	26	22				0	−43	43		h,7,4,	
10	−17	18	13	11	13							2	−22	24	2	−15	18
14	10	12	14	−22	22		h,4,4					4	40	36	3	7	10
15	5	7	15	6	8	1	13	14				6	9	13	4	−6	8
16	11	12	16	8	11	4	−9	11				8	−24	25	5	15	17
17	8	9	17	5	6	6	11	16				10	−20	21	6	11	16
												14	9	10	8	16	18
															10	−7	9

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TABLE 2. (*Continued.*)

h	F_c	$\|F_o\|$	h	F_c	$\|F_o\|$	h	F_c	$\|F_o\|$	h	F_c	$\|F_o\|$	h	F_c	$\|F_o\|$	h	F_c	$\|F_o\|$
	h,7,5		4	−12	9		h,8,4		5	25	25		h,10,0		6	3	5
1	−22	22	7	6	9	0	−29	26	7	−6	7	0	−27	28	7	−4	4
3	7	8				2	−5	8	9	−22	23	4	22	21		h,10,3	
				h,8,2		4	34	28				6	15	16	0	6	7
	h,7,6		0	−40	36	6	7	10		h,9,2		8	−13	14	1	10	11
2	−10	10	4	36	32	7	−8	8	1	−8	9				3	6	7
			5	−9	9	8	−17	18	6	−6	7		h,10,1		4	5	5
	h,8,0		6	19	22	9	−5	5	9	−4	5	0	−22	22			
0	−27	29	8	−20	22							1	8	11		h,11,0	
2	−20	21	9	11	10		h,8,5			h,9,3		3	12	13	2	23	22
4	20	22	10	−11	15	1	−7	7	1	−26	22	4	−10	10	4	8	8
8	−30	31	12	17	15				3	17	16	5	−11	12			
10	−20	21					h,9,0		5	21	23	7	−9	10		h,11,1	
12	15	15				8	9	11	7	−10	12	8	−7	6	1	−12	13
				h,8,3		10	8	9	9	−18	14				3	8	8
	h,8,1		0	8	8								h,10,2		4	5	4
0	−9	9	3	−13	14		h,9,1			h,9,4		0	−17	19			
1	−7	8	4	6	7	1	−19	19	1	8	7	3	5	6			
2	7	9	11	−5	5	3	15	17	2	5	6	4	19	19			

STRUCTURE DETERMINATION

All atoms in the unit $Cu(H{\cdot}COO)_2$ are in general positions whose fractional co-ordinates are $\pm (x,y,z;\ \frac{1}{2}+x,\frac{1}{2}-y,\bar{z};\ x,\frac{1}{2}-y,\frac{1}{2}+z;\ \frac{1}{2}-x,\bar{y},\frac{1}{2}+z)$. Approximate co-ordinates for the copper and the four oxygen atoms were obtained from a three-dimensional Patterson function. Calculation of structure factors with these co-ordinates gave a discrepancy factor, R, of 0·37. A three-dimensional Fourier synthesis led to positions for the carbon atoms. The structure was refined by successive three-dimensional Fourier syntheses; the co-ordinates of the electron-density maxima were determined by the method of Berghius *et al.*[3] Termination-of-series errors were estimated by the back-shift method.[4] Atomic scattering factors of Berghius *et al.*[5] were used for all atoms, the values for copper being corrected for dispersion.[6] A temperature factor, $\exp(-B\sin^2\theta/\lambda^2)$ with $B = 1{\cdot}2$ Å^2 for the copper atom and $B = 1{\cdot}4$ Å^2 for the other atoms, was applied. Structure factors and Fourier syntheses were calculated on UTECOM, a Deuce digital computor, with programmes written by Dr. J. S. Rollett. The estimated standard deviations of the atomic co-ordinates were calculated by Cruickshank's method.[7] The final atomic parameters together with their root-mean-square estimated standard deviations (σ) are given in Table 1. The observed structure amplitudes and the calculated structure factors are listed in Table 2. The final discrepancy factor, R, for the 510 observed reflections was 0·12.

DISCUSSION

The arrangement of the atoms in a unit cell is illustrated in Fig. 1. There are no discrete molecules or ions in the crystal. Both oxygen atoms of the formate group are joined by covalent bonds to copper atoms and, in this way, the formate group acts as a bridge between copper atoms. As each copper atom is linked to four others by four different formate groups, an infinite three-dimensional network is produced.

The possible bridging arrangements of the carboxyl group in copper(II) compounds have been discussed by Martin and Waterman.[1] Because of the strain involved in the formation of a four-membered ring, the chelate structure (I) was considered unlikely. However, a ring system of this type has been found in carbonatotetramminecobalt(III) bromide.[8] The *syn-syn* (II) and the *anti-anti* configuration (III) are known in copper acetate monohydrate[9] and copper formate tetrahydrate[10] respectively. Anhydrous copper formate provides the first example of the *anti-syn*-arrangement (IV).

A correlation between the bridging arrangement of the carboxyl groups and magnetic behaviour is indicated. The close approach (2·64 Å) of the two copper atoms in the

[3] Berghius, Shoemaker, Donohue, Shomaker, and Corey, *J. Amer. Chem. Soc.*, 1950, **72**, 2328.
[4] Booth, *Proc. Roy. Soc.*, 1946, *A*, **188**, 77.
[5] Berghius, Haanappel, Potters, Loopstra, MacGillavry, and Veenendaal, *Acta Cryst.*, 1955, **8**, 478.
[6] Dauben and Templeton, *Acta Cryst.*, 1955, **8**, 841.
[7] Cruickshank, *Acta Cryst.*, 1949, **2**, 65.
[8] Barclay and Hoskins, unpublished observations.
[9] Van Niekerk and Schoening, *Acta Cryst.*, 1953, **6**, 227.
[10] Kiriyama, Ibamoto, and Matsuo, *Acta Cryst.*, 1954, **7**, 482.

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syn-syn-configuration (II) is said [9] to rationalise the anomalous magnetic behaviour of copper acetate monohydrate ($\mu = 1{\cdot}40$ B.M.). An explanation of the difference in

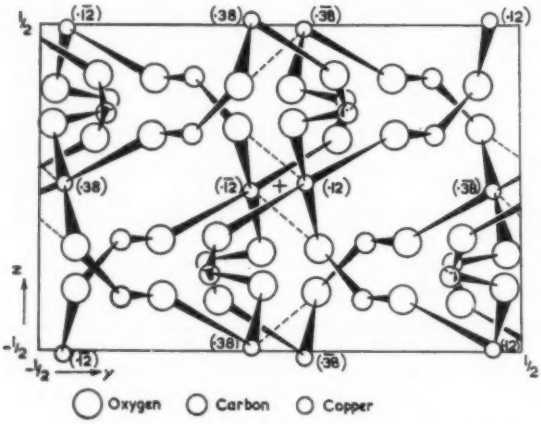

FIG. 1. *Arrangement of the atoms in the unit cell of copper*(II) *formate. The fractional x co-ordinates of the copper atoms are shown in parentheses.*

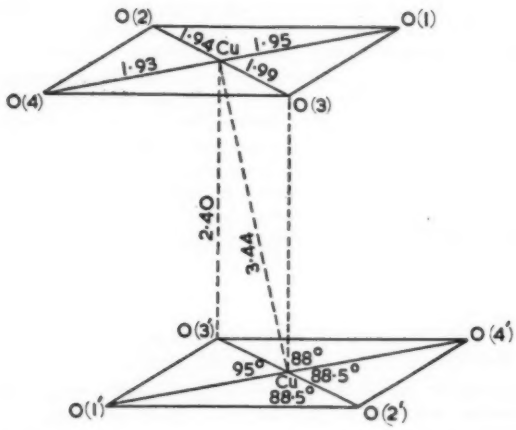

FIG. 2. *Environment of the copper atoms.*

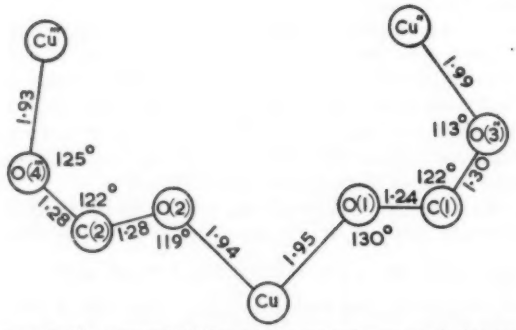

FIG. 3. *Bond lengths* (Å) *and bond angles in the formate bridging groups.*

magnetic susceptibility of the anhydrous and the tetrahydrated copper formate ($\mu = 1{\cdot}90$ and $\mu = 1{\cdot}61$ B.M. respectively) does not appear possible in terms of the distances between copper atoms in these compounds (3·44 and 5·80 Å) respectively.

The copper atom has a distorted tetragonal-pyramidal co-ordination. Four oxygen atoms are in a plane containing the copper atom with a fifth at a greater distance along a line which makes an angle of 31° with the normal to this plane. Two copper atoms share

(I) Chelate (II) *syn-syn* (III) *anti-anti* (IV) *anti-syn*

oxygen atoms to form a type of bimolecular unit (see Figs. 1 and 2). The distance between these atoms is much shorter (3·44 Å) than between any other pair of copper atoms (greater than 4·6 Å). Similar bimolecular arrangements have been reported for *NN'*-ethylenebis-(salicylideneiminato)copper(II),[11] bis(dimethylglyoximato)copper(II),[12] and dichloro(dimethylglyoxime)copper(II).[13]

The bond distances and angles are listed in Table 3 and are shown diagrammatically in Figs. 2 and 3.*

The Cu–O(3) bond is significantly longer (1·99 Å) than the other planar Cu–O bonds (1·94 Å). This might be expected as the O(3) atom is bonded to two copper atoms while the others have only one copper atom as a near neighbour. In Table 4 the copper–oxygen

TABLE 3. *Bond distances and angles.*

Bond	Length (Å)	σ (Å)	Angle	Value	σ
Cu–O(1)	1·945	0·009	O(1)–Cu–O(2)	89°	1°
Cu–O(2)	1·942	0·009	O(1)–Cu–O(3)	95	1
Cu–O(3)	1·986	0·008	O(2)–Cu–O(4)	89	1
Cu–O(4)	1·928	0·010	O(3)–Cu–O(4)	88	1
C(1)–O(1)	1·235	0·013	O(1)–C(1)–O(3″)	122	1
C(1)–O(3″)	1·295	0·013	O(2)–C(2)–O(4‴)	122	1
C(2)–O(2)	1·278	0·014			
C(2)–O(4‴)	1·284	0·015	Cu–O(1)–C(1)	130	1
			Cu–O(2)–C(2)	119	1
Cu–O(3′)	2·397	0·008	Cu″–O(3″)–C(1)	113	1
			Cu‴–O(4‴)–C(2)	125	1
Cu–Cu′	3·435	0·004			

TABLE 4. *Copper–oxygen bond lengths.**

Compound	Cu–O bond length (Å)	Compound	Cu–O bond length (Å)
Copper(II) formate	1·94, 1·99	Bisbiuretcopper(II) chloride	1·92
Monopyridinecopper(II) acetate [a]	1·95	Anhydrous copper nitrate [g]	1·9
Linarite [b]	1·93	Copper fluoride dihydrate [h]	1·93
NN'-Propylenebis(salicylideneiminato) copper(II) [c]	1·88, 1·94	Callaghanite [i]	2·00
		Chalkomenite [j]	1·93
NN'-Ethylenebis(salicylideneiminato)-copper(II) [c]	1·91, 2·03	Azurite [k]	1·88, 1·98
		Barium copper formate [l]	1·97, 2·18
Copper salicylate tetrahydrate [d]	1·84, 1·92		
Meta-zeunerite [e]	2·14		

* For values reported before 1956 see Sutton *et al.*, " Tables of Interatomic Distances and Configuration in Molecules and Ions," *Chem. Soc. Special Publ. No.* 11, London, 1959.

a, Unpublished work. *b*, Bachman and Zemann, *Naturwiss.*, 1960, **8**, 177. *c*, Llewellyn and Waters, *J.*, 1960, 2639. *d*, Hanic and Michalov, *Acta Cryst.*, 1960, **13**, 299. *e*, Hanic, *Czech. J. Phys.*, 1960, **10**, *B*, 169. *f*, Freeman, Smith, and Taylor, *Nature*, 1959, **184**, 707. *g*, Wallwork, *Proc. Chem. Soc.*, 1959, 311. *h*, Geller and Bond, *J. Chem. Phys.*, 1958, **29**, 925. i, Brunton, Steinfink, and Beck, *Acta Cryst.*, 1958, **11**, 169. *j*, Gattow, *ibid.*, p. 377. *k*, Gattow and Zemann, *ibid.*, p. 866. *l*, Rao, Sundarama, and Rao, *Z. Krist.*, 1958, **110**, 231.

bond lengths are compared with those reported previously. The C(1)–O(1) bond length appears to differ from the other carbon–oxygen distances. However, it is probable

* The co-ordinates of the atoms marked with primes are related to those listed in Table 1 in the following way: A′ $(\bar{x}, \bar{y}, \bar{z})$; A″ $(x, \frac{1}{2} - y, \frac{1}{2} + z)$; A‴ $(\frac{1}{2} - x, \bar{y}, \frac{1}{2} + z)$.

[11] Hall and Waters, *J.*, 1960, 2644.
[12] Frasson, Bardi, and Bezzi, *Acta Cryst.*, 1959, **12**, 201.
[13] Barclay, unpublished observations.

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that the estimated standard deviation is too small and that the mean value of 1·273 Å would better represent the carbon–oxygen bond length. The values reported previously for carbon–oxygen bond length and oxygen–carbon–oxygen bond angles in formates are listed in Table 5 for comparison.

The copper atom and its four nearest neighbours are in a plane the equation for which (calculated by the method of least squares) is $0{\cdot}572x + 0{\cdot}521y - 0{\cdot}633z - 1{\cdot}191 = 0$. The deviations of these atoms from the plane [Cu, 0·007; O(1), 0·03; O(2), 0·03; O(3), 0·03; O(4), 0·03 Å] are all within the experimental error. The Cu–O(2)–C(2)–O(4‴)–Cu‴ grouping is planar, but the similar Cu–O(1)–C(1)–O(3″)–Cu″ group is not, presumably owing to the interaction between O(3) and a second copper atom. The equations for the least-squares planes (and the deviations from these planes) are:

$$0{\cdot}556x - 0{\cdot}282y - 0{\cdot}782z - 0{\cdot}732 = 0$$
[Cu, 0·002; O(2), 0·01; C(2), 0·01; O(4‴), 0·01; Cu‴, 0·006 Å]
$$0{\cdot}503x - 0{\cdot}594y - 0{\cdot}628z - 1{\cdot}178 = 0$$
[Cu, 0·07; O(1), 0·12; C(1), 0·04; O(3″), 0·10; Cu″, 0·01 Å]

Orgel and Dunitz [14] have listed three types of stereochemical arrangements found in copper(II) compounds, namely, distorted octahedral with four shorter and two longer bonds, square planar, and tetrahedral. To these types should be added tetragonal-pyramidal (with four shorter and one longer bond) and the binuclear compounds. Anhydrous copper formate and three other examples of tetragonal-pyramidal co-ordination which involve a bimolecular unit have been mentioned above (p. 3293). Callaghanite,[15] chalkomenite,[16] tetramminecopper(II) sulphate monohydrate,[17] and *NN'*-propylenebis-(salicylideneiminato)copper(II) monohydrate [18] have a tetragonal-pyramidal configuration about the copper atom without a bimolecular association. Copper(II) acetate mono-

TABLE 5. *Bond lengths and angles in formates.**

Compound	C–O bond length (Å)	O–C–O bond angle	Compound	C–O bond length (Å)	O–C–O bond angle
Anhydrous copper formate	1·27	122°	Barium copper formate [b] ...	1·23, 1·43	124°
Strontium formate dihydrate [a]	1·21, 1·24	124, 127	Copper formate tetrahydrate [10]	1·25	120

* See footnote * of Table 4.

a, Osaki, *Ann. Reports Sci. Works, Osaka Univ.*, 1958, **6**, 13; *b*, Rao, Sundarama, and Rao, *Z. Krist.*, 1958, **110**, 231.

hydrate [9] and monopyridinecopper(II) acetate [19] are examples of binuclear compounds in which the copper atom has four short and one long bond with a second copper atom in the sixth " octahedral " site. In bis(bipyridine)copper(II) iodide, the copper atom forms five bonds which are directed towards the corners of a trigonal bipyramid.[20] These five bonds are of normal covalent length. In all other cases, the fifth and the sixth atom are at greater distances than expected for covalent bonds.

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[14] Orgel and Dunitz, *Nature*, 1957, **179**, 462.
[15] Ref. *i* of Table 4.
[16] Ref. *j* of Table 4.
[17] Mazzi, *Acta Cryst.*, 1955, **8**, 137.
[18] Ref. *c* of Table 4.
[19] Ref. *a* of Table 4.
[20] Barclay and Kennard, *Nature*, in the press.

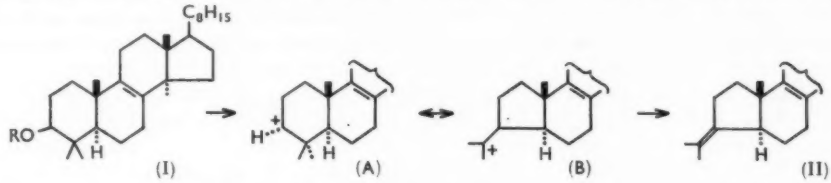
645. *Some Reactions of 4,4,14α-Trimethyl-5α-cholesta-8,24-dien-3α-yl and -3β-yl Toluene-p-sulphonates.*

By G. Bancroft, Y. M. Y. Haddad, and G. H. R. Summers.

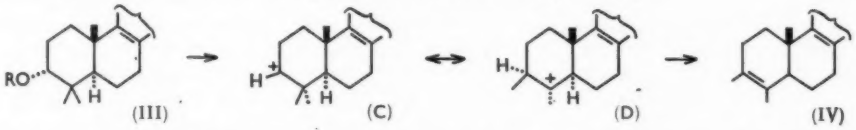
Acetolysis of 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3α-yl toluene-*p*-sulphonate yields 3,4,14α-trimethyl-5α-cholesta-3,8,24-triene and 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3α-yl acetate. A kinetic study of the acetolyses of both these esters shows that their rearrangements involve a unimolecular mechanism.

The behaviour of both toluenesulphonates to basic aluminium oxide and lithium aluminium hydride is described.

In a previous paper [1] we described the acetolyses of the toluene-*p*-sulphonates of 4,4-dimethylcholest-5-en-3β-ol and 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3β-ol (lanosterol) (I; R = *p*-$C_6H_4Me{\cdot}SO_2$). That and subsequent work [2] showed these reactions to involve Wagner rearrangement with cleavage of the 4,5-bond and contraction of ring A to produce principally isopropylidene-A-nor-derivatives * (II). The rearrangement products arise



because 3-substituted 4,4-dimethyl-steroids and terpenes contain an α-substituted neopentyl system which is especially prone to rearrangement.[3] The only other products of acetolysis were the 3β-acetates (I; R = Ac) formed with retention of configuration. The overall reaction pattern was explained by assuming an ionic mechanism proceeding through cations (A, B) either as separate classical entities, or through a non-classical bridged carbonium ion in which the charge is distributed over $C_{(3)}$ and $C_{(4)}$.



By analogy, solvolytic reactions of toluene-*p*-sulphonyl derivatives of 3α-hydroxy-4,4-dimethyl-steroids (III; R = *p*-$C_6H_4Me{\cdot}SO_2$) would also be expected to lead to rearrangement, this time without ring contraction, but with formation of 3,4-dimethyl-steroids (IV) by migration of the 4β-methyl group. This reaction similarly would probably occur through classical cations (C, D) or a non-classical ion.

A decision between the two possibilities in both the 3α- and the 3β-series would depend on whether the rates of solvolysis were normal or accelerated (anchimeric assistance or synartesis). We now show from a kinetic study of the acetolyses of 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3β-yl and -3α-yl toluene-*p*-sulphonate that these 1,2-shifts proceed initially by the classical route. We also describe some further reactions of these compounds which involve rearrangement.

Oxidation of commercial 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3β-ol (I; R = H)

* These are sometimes accompanied by endocyclic isomers.[2]

[1] Haddad and Summers, *J.*, 1959, 769.
[2] Moriarty and Wallis, *J. Org. Chem.*, 1959, **24**, 1274, 1987; Beillmann and Ourisson, *Bull. Soc. chim. France*, 1960, 348.
[3] Ingold, *J.*, 1953, 2845.

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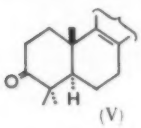
with chromium trioxide in acetone or in pyridine gave 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3-one (V), which had been previously prepared [4] in an impure form by oxidation of lanosterol with chromium trioxide in acetic acid followed by dehydrogenation with copper bronze. Oppenauer oxidation of the alcohol (I; R = H) failed to give any of the ketone (V). Lithium aluminium hydride or sodium borohydride reduced 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3-one (V) to 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3α-ol (III; R = H) (5% and 7%) and the 3β-alcohol (I; R = H) (86% and 92%): the latter alcohol was used in all subsequent reactions. This result agrees with Cavalla's observation [5] that reduction of 4,4,14α-trimethyl-5α-cholest-8-en-3-one gave an almost quantitative yield of the 3β-alcohol, though Huffman [6] obtained a 69% yield of the 3α-alcohol. Huffman's assignment of orientation is, however, based on incorrect conclusions drawn from conformational arguments and dehydration experiments. Reduction of the ketone (V) with aluminium isopropoxide gave 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3α-ol (35%). The alcohol (III; R = H) was characterised by hydrogenation of its acetate to the known 4,4,14α-trimethyl-5α-cholest-8-en-3α-yl acetate.[7,8] Similar reduction of 4,4-dimethyl-5α-cholestan-3-one [9] gave 4,4-dimethyl-5α-cholestan-3α-ol (42%). Oppenauer oxidation of 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3α-ol (III; R = H) gave the ketone (V) (33%). This disparity in the oxidation behaviour of the 3α- and the 3β-alcohol agrees with the hydrolysis behaviour of analogous acetates [10] and is in accord with their steric environment.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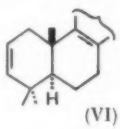
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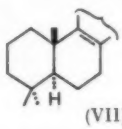
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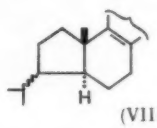
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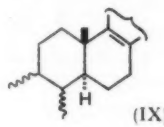

(IX)

Because of the tedious chromatographic separation of the epimeric 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3-ols (I and III; R = H) alternative methods for the preparation of the 3α-alcohol (III; R = H) were examined. It has recently been shown [11] that epimerisation of equatorial steroidal toluene-*p*-sulphonates on aluminium oxide sometimes provides a useful method for obtaining the less accessible axial alcohols. Adsorption of 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3β-yl toluene-*p*-sulphonate (I; R = *p*-$C_6H_4Me{\cdot}SO_2$) on a basic alumina column for three days gave a hydrocarbon mixture, difficultly separable into 4,4,14α-trimethyl-5α-cholesta-2,8,24-triene (VI) and 3-isopropylidene-14α-methyl-A-nor-5α-cholesta-8,24-diene (II). A similar result was obtained on treating the toluenesulphonate (I; R = *p*-$C_6H_4Me{\cdot}SO_2$) with dimethylformamide.[12] A similar result was also obtained with 4,4,14α-trimethyl-5α-cholest-8-en-3β-yl toluene-*p*-sulphonate,[8] and these observations contrast with the behaviour of the esters of the α- and β-amyrins and lupeol.[11] Decomposition of 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3α-yl toluene-*p*-sulphonate (III; R = *p*-$C_6H_4Me{\cdot}SO_2$) on basic alumina also gave a hydrocarbon mixture of (VI) and the rearranged hydrocarbon, 3,4,14α-trimethyl-5α-cholesta-3,8,24-triene (IV). In neither case was an inverted alcohol obtained (cf. cholesteryl toluene-*p*-sulphonate [11]). The structure of the unsaturated hydrocarbon (VI) was proved by its preparation from 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3β-ol (I; R = H) by pyrolysis of its benzoate and by its hydrogenation to 4,4,14α-trimethyl-5α-cholest-8-ene

[4] Ruzicka, Denss, and Jeger, *Helv. Chim. Acta*, 1945, **28**, 759.
[5] Cavalla, Ph.D. Thesis, London, 1951.
[6] Huffman, *J. Org. Chem.*, 1959, **24**, 447.
[7] Marker and Wittle, *J. Amer. Chem. Soc.*, 1937, **59**, 2289; Allsop, Cole, White, and Willis, *J.*, 1956, 4868.
[8] McGhie, Palmer, Rosenberger, Birchenough, and Cavalla, *Chem. and Ind.*, 1959, 1221.
[9] Beton, Halsall, Jones, and Phillips, *J.*, 1957, 753.
[10] Ruzicka and Gubser, *Helv. Chim. Acta*, 1945, **28**, 1054, 1372.
[11] Chang and Blickenstaff, *Chem. and Ind.*, 1958, 590; Douglas, Ellington, Meakins, and Swindells, *J.*, 1959, 1720.
[12] Chang and Blickenstaff, *J. Amer. Chem. Soc.*, 1958, **80**, 2906.

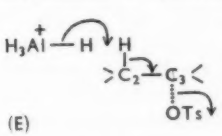
(VII). Attempted preparation from 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3-one (V) by the Bamford–Stevens reaction [13] surprisingly gave a quantitative yield of the 3-isopropylidene-14α-methyl-A-nor-5α-cholesta-8,24-diene (II). The occurrence of Wagner rearrangement has also been encountered in the alkaline decomposition of the toluene-*p*-sulphonylhydrazones of camphor [13] and hecogenin.[14]

Acetolysis of 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3β-yl toluene-*p*-sulphonate (I; R = *p*-$C_6H_4Me{\cdot}SO_2$) with potassium acetate in acetic acid at 95° for 3 hr. has already been shown [1] to yield, after hydrolysis, 3-isopropylidene-14α-methyl-A-nor-5α-cholesta-8,24-diene (II) and the parent alcohol (I; R = H). Similar treatment of 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3α-yl toluene-*p*-sulphonate (III; R = *p*-$C_6H_4Me{\cdot}SO_2$) gave, after hydrolysis, 3,4,14α-trimethyl-5α-cholesta-3,8,24-triene (IV) (52%) and the parent alcohol (III; R = H) (15%). Again there was no evidence of inversion without rearrangement, and this reaction represents another example contrasting with the accepted behaviour of nucleophilic reaction at position 3 in saturated steroids.[15] Similarly 4,4,14α-trimethyl-5α-cholest-8-en-3α-yl toluene-*p*-sulphonate and 4,4-dimethyl-5α-cholestan-3α-yl toluene-*p*-sulphonate gave, respectively, 3,4,14α-trimethyl-5α-cholesta-3,8-diene and 3,4-dimethyl-5α-cholest-3-ene.

The structures of the rearranged trimethyl hydrocarbons are assigned by analogy, since the product from the cholestane series proved to be identical with the 3,4-dimethylcholest-3-ene synthesised by Beton, Halsall, Jones, and Phillips.[9] The hydrocarbon (IV) was also obtained, mixed with 4,4,14α-trimethyl-5α-cholesta-2,8,24-triene (VI), by dehydration of 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3α-ol (III; R = H) in hexane with phosphorus pentachloride.

Catalytic hydrogenation of 3-isopropylidene-14α-methyl-A-nor-5α-cholest-8-ene has previously been reported [6] as giving a 14α-methyl-A-norcholestane compound in which the normally inert 8,9-double bond [16,17] has been reduced. Repetition of this reduction with this compound and with 3-isopropylidene-14α-methyl-A-nor-5α-cholesta-8,24-diene (II) showed this finding to be incorrect since these hydrocarbons absorbed one and two mol. of hydrogen, respectively, to give 3ξ-isopropyl-14α-methyl-A-nor-5α-cholest-8-ene (VIII) in which presumably the isopropyl group is β-orientated. 3,4,14α-Trimethyl-5α-cholesta-3,8,24-triene (IV) and -3,8-diene, on catalytic hydrogenation, absorbed two and one mol. of hydrogen, respectively, to give 3ξ,4ξ,14α-trimethyl-5α-cholest-8-ene (IX).

Reduction of 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3β-yl toluene-*p*-sulphonate (I; R = *p*-$C_6H_4Me{\cdot}SO_2$) with lithium aluminium hydride for 30 hr. gave principally the isopropylidene derivative (II), with some parent alcohol (I; R = H). It seems that the mechanism of reduction involved is akin to that of solvolytic reactions of the ester (I; R = *p*-$C_6H_4Me{\cdot}SO_2$) (cf. reduction of toluene-*p*-sulphonic esters of 3β-hydroxy-Δ⁵-steroids [18]). Reduction of the toluene-*p*-sulphonates of the alcohol (III; R = H) and of 4,4,14α-trimethyl-5α-cholest-8-en-3α-ol for 40 hr. surprisingly gave only 4,4,14α-trimethyl-5α-cholesta-2,8,24-triene (VI) and -2,8-diene and some of the parent alcohols but no isolable rearrangement products. The ready formation of the 2,3-double bond appears to be a consequence of the geometry of compound (III), the facility of the elimination involving four coplanar centres in the transition state (E) (cf. Cram [19] and Evans *et al.*[20]).



(E)

[13] Bamford and Stevens, *J.*, 1952, 4735.
[14] Elks, Phillipps, Taylor, and Wyman, *J.*, 1954, 1739; Hirschmann, Snoddy, Hiskey, and Wendler, *J. Amer. Chem. Soc.*, 1954, **76**, 4013.
[15] Shoppee, *J.*, 1946, 1138; Bridgewater and Shoppee, *J.*, 1953, 1709.
[16] Simonsen and Ross, " The Terpenes," Cambridge Univ. Press, 1957, Vol. IV, p. 39.
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To obtain further detail about the proposed mechanisms of rearrangement we next examined kinetically acetolysis of the toluene-*p*-sulphonates (I, III; R = *p*-$C_6H_4Me{\cdot}SO_2$). Results of typical runs are given in Tables 1 and 2. Table 3 summarises the results obtained in the kinetic studies. These measurements indicate both acetolyses to be unimolecular and thus to involve a rate-determining heterolysis. The rate of solvolysis

TABLE 1. *Acetolysis of* 0·0174M-4,4,14α-*trimethyl*-5α-*cholesta*-8,24-*dien*-3β-*yl toluene*-p-*sulphonate in anhydrous acetic acid at* 76·75° ± 0·05°.

Time (min.)	15	28	43	58	73
10^3k (min.$^{-1}$)	6·15	6·17	6·28	6·19	6·26

Initial specific rate constant = 6·21 × 10^{-3} min.$^{-1}$.

TABLE 2. *Acetolysis of* 0·0201M-4,4,14α-*trimethyl*-5α-*cholesta*-8,24-*dien*-3α-*yl toluene*-p-*sulphonate in anhydrous acetic acid at* 76·95° ± 0·05°.

Time (min.)	15	30	45	65	80
10^3k (min.$^{-1}$)	17·26	15·85	14·87	13·57	12·87

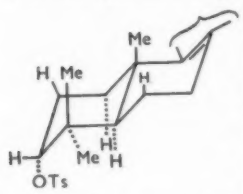
Initial specific rate constant = 17·1 × 10^{-3} min.$^{-1}$.

TABLE 3. *Rates of acetolysis of* 0·01—0·2M-*solutions of* 4,4,14α-*trimethyl*-5α-*cholesta*-8,24-*dien*-3β-*yl and* -3α-*yl toluene*-p-*sulphanate.*

3β-Ester			3α-Ester		
Temp.	* Added acetate (M)	10^3k (min.$^{-1}$) (average)	Temp.	* Added acetate (M)	10^3k (min.$^{-1}$) (average)
76·8	—	6·30	76·9	—	16·9
76·8	0·02	6·30	77·0	0·02	15·7
77·3	0·01	4·95	77·3	0·01	15·4
86·6	—	17·8	67·6	—	5·20
86·5	0·02	16·0	68·3	0·02	5·40
60·1	—	0·92	59·7	—	2·04
60·3	0·02	1·03	59·8	0·02	2·27
			55·5	0·02	1·26

* Diphenylguanidinium acetate.

of the axial 3α-ester is ~3 times greater than that of the equatorial 3β-ester. This difference is similar to that met in the acetolyses of the 5α-cholestanyl toluene-*p*-sulphonates.[21] Thus 5α-cholestan-3α-yl toluene-*p*-sulphonate is solvolysed ~6 times faster than its 3β-isomer at 75°. Attempts have been made to correlate solvolysis rate differences in rigid cyclohexane systems with conformational effects,[21,22,23] and application of these ideas to our problem supports them. The greater reactivity of 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3α-yl toluene-*p*-sulphonate (III; R = *p*-$C_6H_4Me{\cdot}SO_2$) can be related, first, to two axial (1,3-H) non-bonded interactions on the α-side of ring A, and, secondly, to four axial (1,3-Me–H) and one axial (1,3-Me–Me) interactions on the β-side of the molecule. Any relief of strain on the α-face, by a minor movement of the toluene-*p*-sulphonate group away from the axial 1- and 5-hydrogen atoms would be opposed by a stiffening of ring A by the interactions on the β-face. Reactions of both the toluene-*p*-sulphonates are probably influenced by conformational long range effects, although not identically so. From the work of Barton *et al.*[24] it would be expected that the 8,9-double bond may bring about major effects at position 3, but as yet no quantitative information is available.



The above steric and structural factors very probably account for the relatively

[21] Moritani, Nishida, and Murakami, *J. Amer. Chem. Soc.*, 1959, **81**, 3420.
[22] Nishida, *J. Amer. Chem. Soc.*, 1960, **82**, 4290.
[23] Winstein and Holness, *J. Amer. Chem. Soc.*, 1955, **77**, 5562.
[24] Barton, McCapra, May, and Thudium, *J.*, 1960, 1297.

slightly faster acetolysis of the toluene-*p*-sulphonate esters (I, III; R = *p*-$C_6H_4Me{\cdot}SO_2$) than of cyclohexyl toluene-*p*-sulphonate ($k = 2{\cdot}56 \times 10^{-3}$ min.$^{-1}$ at 79°) and the 5α-cholestan-3-yl toluene-*p*-sulphonates (3α, $k = 10{\cdot}2 \times 10^{-3}$ min.$^{-1}$; 3β, $k = 1{\cdot}7 \times 10^{-3}$ min.$^{-1}$; at 75·3°). The occurrence of these rearrangements by a " normal rate " process and not by one involving synartesis [3] seemingly excludes the formation of bridged carbonium-ion intermediates. Even so we think that there are legitimate objections to abandoning this mechanistic pathway altogether. It is difficult to account for the absence of inverted 3-acetates, 3,4,14α-trimethylcholesta-8,24-dien-4-yl acetates, and 3,4,14α-trimethylcholesta-4,8,24-triene. Moriarty and Wallis [2] have suggested that in the hydrolysis of 4,4-dimethylcholest-5-en-3β-yl toluene-*p*-sulphonate in aqueous acetone containing potassium acetate the formation of 4,4-dimethylcholesterol may be due to oxygen–sulphur bond fission rather than alkyl–oxygen bond fission. We think that this mechanism is not applicable to the above acetolyses since the products of retention of configuration are acetates. These difficulties can be resolved if it is assumed that the initial classical ions (A and C) rearrange to non-classical bridged ions of greater thermodynamic stability, at a rate which is fast compared with that of the initial heterolysis. The absence of any tertiary acetates * derived from ions (B and D) or bridged ions is probably due, first, to the weak nucleophilic power of the acetate ion and, secondly, to preferential stabilisation of weakly solvated ions by loss of a proton rather than by co-ordination with an acetate ion.

These preliminary kinetic results show some unusual features. In acetolysis of 4,4,14α-trimethylcholesta-8,24-dien-3β-yl toluene-*p*-sulphonate (I; R = *p*-$C_6H_4Me{\cdot}SO_2$) (Table 1) good first-order constants were obtained, showing little downward drift with time, whereas for acetolysis of 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3α-yl toluene-*p*-sulphonate (III; R = $C_6H_4Me{\cdot}SO_2$) (Table 2) the first-order constants show a marked downward drift. The solvolyses of both compounds were slower after addition of diphenylguanidinium acetate. Also the entropy of activation for the first reaction was negative ($\Delta S = -3{\cdot}1$ cal. mole^{-1} deg.$^{-1}$), whilst in the second reaction it was positive ($\Delta S = +4{\cdot}6$ cal. mole^{-1} deg.$^{-1}$). Inferences to be drawn from these observations will be deferred for a more thorough investigation of salt effects in these reactions and until the kinetics of acetolysis of related systems (*e.g.*, 5α-cholest-8-en-3α-yl and -3β-yl toluene-*p*-sulphonates) have been studied.

Experimental

The aluminium oxide used, unless stated otherwise, was Spence type H. $[\alpha]_D$ are for chloroform solutions.

4,4,14α-Trimethyl-5α-cholesta-8,24-dien-3-one.—(*a*) 4,4,14α-Trimethyl-5α-cholesta-8,24-dien-3β-ol (lanosterol) (20 g.) in acetone (350 ml.) was stirred at room temperature and treated with a solution of chromium trioxide in sulphuric acid. The addition was stopped when the solution became light orange. After 0·5 hr. the solution was diluted with water and filtered, and the solid obtained was extracted with ether and worked up in the usual way, to give an oil (16 g.) which solidified. Repeated crystallisation from methanol–ether gave 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3-one, m. p. 107—109°, $[\alpha]_D$ +71° (*c* 1·0). Ruzicka, Denss, and Jeger [4] give m. p. 82—82·5°, $[\alpha]_D$ +81·7°.

(*b*) Lanosterol (14·2 g.) in pyridine (284 ml.) was treated with powdered chromium trioxide (14·2 g.) and left for 16 hr. Isolation of the product in the usual way gave an oil which was chromatographed on aluminium oxide (400 g.). Elution with benzene–pentane (1 : 9) (9 × 150 ml.) gave an oil (6·1 g.) which by crystallisation from ether–methanol gave the above ketone, m. p. 111—114°, $[\alpha]_D$ +72° (*c* 0·9). Elution with ether gave lanosterol.

Attempted Oppenauer oxidation of lanosterol gave only starting material.

Reduction of 4,4,14α-Trimethyl-5α-cholesta-8,24-dien-3-one.—(*a*) A solution of 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3-one (2 g.) in ether (200 ml.) was heated with lithium aluminium hydride (700 mg.) for 1·5 hr. The product was chromatographed on aluminium oxide (60 g.).

* 3β-(1-Hydroxy-1-methylethyl)-A-nor-derivatives have been isolated from solvolyses in buffered media and deaminations of 3β-amino-4,4-dimethyl-5α-steroids in aqueous acetic acid. 3β-(1-Hydroxy-1-methylethyl)-A-norcholest-5-ene [2] was in our original paper wrongly considered to be 4,4-dimethyl-3α,5-cyclocholestan-6β-ol.

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Elution with benzene (3 × 100 ml.) gave a solid (109 mg.) which after crystallisation from acetone–methanol gave 4,4,14α-*trimethyl*-5α-*cholesta*-8,24-*dien*-3α-*ol*, m. p. 132—134°, $[\alpha]_D$ +43° (*c* 0·7) (Found: C, 84·6; H, 12·0. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%). Further elution with benzene (15 × 100 ml.), ether–benzene (1 : 9) (5 × 100 ml.), and ether–benzene (1 : 1) (6 × 100 ml.) gave lanosterol (1·73 g.), m. p. 138—141°.

The lanosterol obtained by this method was used in subsequent chemical and kinetic experiments.

(*b*) The ketone (2 g.) in ethanol (150 ml.) was reduced with sodium borohydride (700 mg.) at room temperature. Chromatography of the product gave 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3α-ol (101 mg.), lanosterol (1·3 g.), and unchanged starting material (585 mg.).

(*c*) The ketone (30 g.) in propan-2-ol (400 ml.) was treated with aluminium isopropoxide (40 g.). Reduction was complete in 3 hr. The product was chromatographed on aluminium oxide (500 g.). Elution with benzene (8 × 1 l.) gave 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3α-ol, m. p. 130—131° (10·48 g.). Further elution with benzene gave a mixture (1·45 g.) and then lanosterol (15 g.).

4,4-*Dimethyl*-5α-*cholestan*-3α-*ol and* -3β-*ol*.—4,4-Dimethyl-5α-cholestan-3-one (2 g.) was added to a solution of aluminium isopropoxide (2·5 g.) in propan-2-ol (25 ml.). The mixture was distilled slowly until the distillate was free from acetone, the volume being maintained by addition of propan-2-ol when necessary. The product was chromatographed on aluminium oxide (60 g.). Elution with ether–benzene (1 : 4) (6 × 200 ml.) gave a solid (840 mg.) which by crystallisation from acetone yielded 4,4-dimethyl-5α-cholestan-3α-ol, m. p. 150—151°, $[\alpha]_D$ +5·5° (*c* 1·0) (Found: C, 83·6; H, 12·0. $C_{29}H_{52}O$ requires C, 83·6; H, 12·5%). Elution with ether and chloroform gave 4,4-dimethyl-5α-cholestan-3β-ol (1·1 g.), m. p. 155°, $[\alpha]_D$ +12° (*c* 1·0) (lit.,[25] m. p. 157—158°, $[\alpha]_D$ +11°).

4,14,14α-*Trimethyl*-5α-*cholest*-8-*en*-3α-*yl Acetate*.—Acetylation of 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3α-ol with pyridine–acetic anhydride gave the *acetate* (needles from acetone), m. p. 158—161°, $[\alpha]_D$ +5·5° (*c* 1·3) (Found: C, 81·8; H, 11·4. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%). Hydrogenation of this compound (500 mg.) in acetic acid (50 ml.) in the presence of platinum oxide (110 mg.) gave a solid which on crystallisation from acetone gave 4,4,14α-trimethyl-5α-cholest-8-en-3α-yl acetate, m. p. 169—171°, $[\alpha]_D$ +3·7° (*c* 1·3). Marker and Wittle [7] give m. p. 167·5°.

Treatment of this acetate with lithium aluminium hydride in boiling ether gave 4,4,14α-trimethyl-5α-cholest-8-en-3α-ol, m. p. 136—138° $[\alpha]_D$ +50° (*c* 0·8). Marker and Wittle [7] give m. p. 139°.

4,4,14α-*Trimethyl*-5α-*cholesta*-8,24-*dien*-3α-*yl Toluene*-p-*sulphonate*.—4,4,14α-Trimethyl-5α-cholesta-8,24-dien-3α-ol (5·8 g.) in pyridine (50 ml.) was treated at 0° with toluene-*p*-sulphonyl chloride (5·8 g.) and left at 25° for 40 hr. The solid product, crystallised from ether, had m. p. 143—146°. Recrystallisation from benzene–pentane (1 : 9) gave 4,4,14α-*trimethyl*-5α-*cholesta*-8,24-*dien*-3α-*yl toluene*-p-*sulphonate*, m. p. 144° (decomp.), $[\alpha]_D$ +19° (*c* 1·0) (Found: C, 76·3; H, 9·4. $C_{37}H_{56}O_3S$ requires C, 76·5; H, 9·7%). Another preparation gave a sample of m. p. 126—127° (decomp.), $[\alpha]_D$ +13·7° (*c* 0·9), when crystallised from ethyl acetate.

4,4,14α-*Trimethyl*-5α-*cholest*-8-*en*-3α-*yl Toluene*-p-*sulphonate*.—4,4,14α-Trimethyl-5α-cholest-8-en-3α-ol (2 g.) in pyridine (20 ml.) was treated with toluene-*p*-sulphonyl chloride (2 g.) and left for 3 days. The product, on crystallisation from acetone, gave 4,4,14α-*trimethyl*-5α-*cholest*-8-*en*-3α-*yl toluene*-p-*sulphonate*, m. p. 138—139° (decomp.), $[\alpha]_D$ −4° (*c* 1·1) (Found: C, 76·5; H, 9·7. $C_{37}H_{58}O_3S$ requires C, 76·2; H, 10·0%).

4,4-*Dimethyl*-5α-*cholestan*-3α-*yl Toluene*-p-*sulphonate*.—4,4-Dimethyl-5α-cholestan-3α-ol (1 g.) in pyridine (10 ml.) was treated with toluene-*p*-sulphonyl chloride (1 g.) and left for 4 days. Crystallisation of the product from acetone–methanol gave 4,4-*dimethyl*-5α-*cholestan*-3α-*yl toluene*-p-*sulphonate*, m. p. 156—158° (decomp.), $[\alpha]_D$ −8° (*c* 0·9) (Found: C, 75·8; H, 9·85. $C_{36}H_{58}O_3S$ requires C, 75·1; H, 10·4%).

Acetolysis of 4,4,14α-*Trimethyl*-5α-*cholesta*-8,24-*dien*-3α-*yl Toluene*-p-*sulphonate*.—4,4,14α-Trimethyl-5α-cholesta-8,24-dien-3α-yl toluene-*p*-sulphonate (1 g.) in acetic acid (50 ml.) containing anhydrous potassium acetate (8·5 g.) was heated at 95° for 3 hr. The product, an oil, was hydrolysed by refluxing it with 5% methanolic potassium hydroxide (50 ml.) for 1 hr. The resulting oil was chromatographed on aluminium oxide (40 g.). Elution with pentane (4 × 100 ml.) gave an oily fraction A (558 mg.). Elution with benzene–pentane gave an oil

[25] Mazur and Sondheimer, *J. Amer. Chem. Soc.*, 1958, **80**, 5220.

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(33 mg.). Elution with ether–benzene (1 : 9) (6 × 100 ml.) gave 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3α-ol, m. p. 132—134° (110 mg.); ether and chloroform gave an oil (20 mg.). Fraction A was repeatedly recrystallised from acetone, and successive crops of crystals were obtained with m. p. 100—102°, 106—108° ($[\alpha]_D$ +79°), 109—111° ($[\alpha]_D$ +65·5°). A final recrystallisation gave 3,4,14α-*trimethyl*-5α-*cholesta*-3,8,24-*triene*, m. p. 110—112°, $[\alpha]_D$ +63·7° (*c* 0·95) (Found: C, 88·0; H, 11·8. $C_{30}H_{48}$ requires C, 88·2; H, 11·8%). The residue from the above crystallisations, on further crystallisation from acetone, gave fractions of m. p. 88—100°, $[\alpha]_D$ +92·5°, and m. p. 75—100°, $[\alpha]_D$ +105·5°. This second hydrocarbon could not be further purified and appears to be a mixture of the above compound with 4,4,14α-trimethyl-5α-cholesta-2,8,24-triene.

Acetolysis of 4,4,14α-*Trimethyl*-5α-*cholest*-8-*en*-3α-*yl Toluene*-p-*sulphonate.*—4,4,14α-Trimethyl-5α-cholest-8-en-3α-yl toluene-*p*-sulphonate (1·1 g.) in acetic acid (100 ml.) containing anhydrous potassium acetate (8 g.) was heated at 95° for 3 hr. The product, after hydrolysis, gave an oil which was chromatographed on aluminium oxide (30 g.). Elution with pentane gave an oil which by crystallisation from ether–ethanol gave 3,4,14α-*trimethyl*-5α-*cholesta*-3,8-*diene* (580 mg.), m. p. 90—94°, $[\alpha]_D$ +61·7° (*c* 0·8) (Found: C, 87·2; H, 11·9. $C_{30}H_{50}$ requires C, 87·75; H, 12·25%). Elution with chloroform gave 4,4,14α-trimethyl-5α-cholest-8-en-3α-ol (140 mg.), m. p. 135—138°, $[\alpha]_D$ +45° (*c* 1·2).

Acetolysis of 4,4-*Dimethyl*-5α-*cholestan*-3α-*yl Toluene*-p-*sulphonate.*—The toluene-*p*-sulphonate (500 mg.) in acetic acid (100 ml.) containing anhydrous potassium acetate was heated at 95° for 3 hr. Working up in the usual way gave an oil which was chromatographed on aluminium oxide (20 g.). Elution with pentane gave an oil which by crystallisation from acetone gave 3,4-dimethyl-5α-cholest-3-ene, m. p. 107—108°, $[\alpha]_D$ +6° (*c* 1·1). Beton *et al.*[9] give m. p. 106·5—108°, $[\alpha]_D$ +5°. Elution with chloroform gave 4,4-dimethyl-5α-cholestan-3α-ol (65 mg.), m. p. 150°.

Dehydration of 4,4,14α-*Trimethyl*-5α-*cholesta*-8,24-*dien*-3α-*ol.*—4,4,14α-Trimethyl-5α-cholesta-8,24-dien-3α-ol (1 g.) in light petroleum (b. p. 60—80°; 100 ml.) was shaken with phosphorus pentachloride (1 g.) for 0·5 hr., then added to aluminium oxide in pentane and eluted with pentane. This gave an oil (744 mg.). Repeated crystallisation from acetone gave crops of crystals melting in the range 55—65° to 110—112°. Final recrystallisation of the last fraction from ether gave 3,4,14α-trimethyl-5α-cholesta-3,8,24-triene, $[\alpha]_D$ +55·6° (*c* 0·94), m. p. 114—116° undepressed on admixture with the specimen obtained from the acetolysis. A fraction of m. p. 64—68°, clearing at 90°, had $[\alpha]_D$ +97·5°, indicating that this reaction again gave a mixture of 3,4,14α-trimethyl-5α-cholesta-3,8,24-triene and 4,4,14α-trimethyl-5α-cholesta-2,8,24-triene.

4,4,14α-*Trimethyl*-5α-*cholesta*-2,8,24-*triene.*—Pyrolysis of lanosteryl benzoate at 320° under reduced pressure gave an oil which was filtered through a column of aluminium oxide. Crystallisation from ethyl acetate–acetone gave rods, m. p. 69—71°, $[\alpha]_D$ +129°, and recrystallisation from acetone gave 4,4,14α-*trimethyl*-5α-*cholesta*-2,8,24-*triene*, m. p. 76—78°, $[\alpha]_D$ +126° (*c* 0·9) (Found: C, 87·9; H, 11·4. $C_{30}H_{48}$ requires C, 88·2; H, 11·8%).

3-*Isopropylidene*-14α-*methyl*-A-*nor*-5α-*cholesta*-8,24-*diene.*—4,4,14α-Trimethyl-5α-cholesta-8,24-dien-3-one (2 g.) was treated with toluene-*p*-sulphonhydrazide (2 g.) in refluxing ethanol for 1 hr. The product, a gel, was extracted with methylene dichloride–ether, and worked up in the usual way; it gave a jelly. The crude dried material had m. p. 238—240° (decomp.). This material in refluxing ethylene glycol (350 ml.) was treated during 1 hr. with sodium (12 g.). After a further 3 hours' refluxing, the solution was cooled, treated with ethanol to destroy the excess of sodium, and worked up in the usual way. The oily product was filtered in pentane through a column of aluminium oxide in pentane. Repeated crystallisation of the still oily product from the eluate gave 3-isopropylidene-A-nor-5α-cholesta-8,24-diene, m. p. and mixed m. p. 136—140°, $[\alpha]_D$ +77·7° (*c* 1·2).

Reduction of the Toluene-p-*sulphonates by Lithium Aluminium Hydride.*—(1) 4,4,14α-*Trimethyl*-5α-*cholesta*-8,24-*dien*-3β-*yl toluene*-p-*sulphonate.* The toluene-*p*-sulphonate (2 g.) in ether (500 ml.) was heated under reflux with lithium aluminium hydride (2 g.) for 24 hr. The product, an oil, was chromatographed on aluminium oxide (100 g.). Elution with pentane (3 × 50 ml.) gave an oil (1·29 g.) which crystallised from ethyl acetate, to give 3-isopropylidene-14α-methyl-A-nor-5α-cholesta-8,24-diene, m. p. 138—140°, $[\alpha]_D$ +84° (*c* 1·2). The oily residues gave a fraction of m. p. 45—65°, which indicated the presence of another hydrocarbon. Elution with ether and chloroform gave lanosterol (165 mg.).

(2) 4,4,14α-*Trimethyl*-5α-*cholesta*-8,24-*dien*-3α-*yl toluene*-p-*sulphonate.* The toluene-*p*-sulphonate (1·83 g.) in ether (500 ml.) was heated under reflux with lithium aluminium hydride

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(2·1 g.) for 39 hr. The product, an oil (1·33 g.), was chromatographed on aluminium oxide (70 g.). Elution with pentane gave an oil (876 mg.) which on crystallisation from acetone gave 4,4,14α-trimethyl-5α-cholesta-2,8,24-triene, $[\alpha]_D$ +118° (*c* 1·0), m. p. 78—79° undepressed on admixture with the specimen obtained from the pyrolysis of lanosteryl benzoate. The infrared curves of these two products were identical. Elution with ether gave 4,4,14α-trimethyl-5α-cholesta-8,24-dien-3α-ol (384 mg.).

(3) *4,4,14α-Trimethyl-5α-cholest-8-en-3α-yl toluene-*p*-sulphonate.* The toluene-*p*-sulphonate (540 mg.) in ether (100 ml.) was heated under reflux with lithium aluminium hydride (540 mg.) for 40 hr. The oily product was chromatographed on aluminium oxide (20 g.). Elution with pentane gave an oil (234 mg.) which on repeated crystallisation from chloroform in methanol gave 4,4,14α-trimethyl-5α-cholesta-2,8-diene, m. p. 80—81°, $[\alpha]_D$ +124·5° (*c* 0·9). Elution with ether gave 4,4,14α-trimethyl-5α-cholest-8-en-3α-ol (117 mg.), m. p. 140°.

*Reaction of the Toluene-*p*-sulphonates on Alkaline Aluminium Oxide.*—(1) *4,4,14α-Trimethyl-5α-cholesta-8,24-dien-3β-yl toluene-*p*-sulphonate.* The toluene-*p*-sulphonate (1·1 g.) in benzene was adsorbed on a column of basic aluminium oxide (Woelm; 100 g.). More benzene (10 ml.) was run on to the column which was then stoppered for 3 days. Elution with benzene gave an oil (696 mg.) which, on repeated crystallisation from ether–ethanol, gave the less soluble 3-isopropylidene-14α-methyl-A-nor-5α-cholesta-8,24-diene, m. p. 136—139°. Crystallisation of the residues from ethanol finally gave needles, m. p. 72—76°, $[\alpha]_D$ +112°, of impure 4,4,14α-trimethyl-5α-cholesta-2,8,24-triene. Treatment of this toluene-*p*-sulphonate with dimethylformamide at 78° for 72 hr. gave an oil from which after many recrystallisations the above pair of hydrocarbons was isolated in small quantity.

(2) *4,4,14α-Trimethyl-5α-cholesta-8,24-dien-3α-yl toluene-*p*-sulphonate.* The toluene sulphonate (1·1 g.) was treated as in the previous experiment for 8 days. Elution with benzene gave an oil (556 mg.), whilst chloroform gave the 3α-alcohol (257 mg.), m. p. 131—132°. The oil was fractionally crystallised from ethyl acetate–methanol, to give 3,4,14α-trimethyl-5α-cholesta-3,8,24-triene, m. p. 106—110°, $[\alpha]_D$ +62°, and impure 4,4,14α-trimethyl-5α-cholesta-3,8,24-triene, m. p. 69—74°, $[\alpha]_D$ +105°.

4,4,14α-Trimethyl-5α-cholest-8-ene.—4,4,14α-Trimethyl-5α-cholesta-2,8,24-triene (325 mg.) [obtained from the lithium aluminium hydride reduction (above) of the 3α-toluene-*p*-sulphonate] in acetic acid–ethyl acetate (1 : 1) (60 ml.) was hydrogenated in the presence of platinum oxide (113 mg.). The oily product was filtered in pentane through aluminium oxide; it then crystallised from acetone, giving 4,4,14α-trimethyl-5α-cholest-8-ene, m. p. 76—78°, $[\alpha]_D$ +63·5° (*c* 1·0), undepressed in m. p. on admixture with an authentic sample of m. p. 74·5—75·5°, $[\alpha]_D$ +65·4° (*c* 1·2).

3ξ-Isopropyl-14α-methyl-A-nor-5α-cholest-8-ene.—(*a*) 3-Isopropylidene-14α-methyl-A-nor-5α-cholesta-8,24-diene (315 mg.) in acetic acid–ethyl acetate (1 : 1) (60 ml.) was hydrogenated in the presence of platinum oxide (129 mg.). Two mol. of hydrogen were absorbed by the compound. The oily product, after filtration of a pentane solution through a column of aluminium oxide, crystallised from ether–ethanol, to give *3ξ-isopropyl-14α-methyl-5α-cholest-8-ene*, m. p. 63—65°, $[\alpha]_D$ +49·6° (*c* 1·05) (Found: C, 87·0; H, 12·5. $C_{30}H_{52}$ requires C, 87·3; H, 12·7%). (*b*) 3-Isopropylidene-14α-methyl-A-nor-5α-cholest-8-ene (143 mg.) in ethyl acetate–acetic acid (1 : 1) (60 ml.) was hydrogenated in the presence of platinum oxide (50 mg.). One mol. of hydrogen was absorbed by the compound. Crystallisation of the product from ether–ethanol gave 3-isopropyl-14α-methyl-A-nor-5α-cholest-8-ene, m. p. 60—64°, $[\alpha]_D$ +48·5° (*c* 0·93).

3ξ,4ξ,14α-Trimethyl-5α-cholest-8-ene.—(*a*) 3,4,14α-Trimethyl-5α-cholesta-3,8,24-triene (288 mg.) in ethyl acetate–acetic acid (1 : 1) (60 ml.) was hydrogenated in the presence of platinum oxide (101 mg.). Two mol. of hydrogen were absorbed by the compound. Filtration of a pentane solution of the product through aluminium oxide in pentane, followed by crystallisation, gave *3ξ,4ξ,14α-trimethyl-5α-cholest-8-ene*, m. p. 98—101°, $[\alpha]_D$ +78° (*c* 1·0) (Found: C, 87·3; H, 12·4. $C_{30}H_{52}$ requires C, 87·3; H, 12·7%).

(*b*) 3,4,14α-Trimethyl-5α-cholesta-3,8-diene (61 mg.) in ethyl acetate–acetic acid (1 : 1) (50 ml.) was hydrogenated in the presence of platinum oxide (63 mg.). One mol. of hydrogen was absorbed. Crystallisation of the product several times from acetone gave 3β,4β,14α-trimethyl-5α-cholest-8-ene, m. p. 99—103°, $[\alpha]_D$ +70° (*c* 1·1).

Kinetic Measurements.—Preliminary runs established that the reactions proceeded at convenient rates in the temperature range 60—90°. " AnalaR " glacial acetic acid was employed as solvent, and solutions were made up by weight in stoppered flasks. Constant

temperature was maintained by using a vapour-thermostat in which chloroform, ethanol, hexane, or trichloroethylene were employed as boiling liquid. Temperature fluctuations during a day did not exceed 0·05°. The liberated toluene-*p*-sulphonic acid was determined by withdrawing 5 ml. portions at intervals and adding a known excess of diphenylguanidinium acetate in acetic acid as base. The excess of base was titrated against a standard solution (0·05 or 0·01M) of perchloric acid in acetic acid. A 0·1% solution of quinaldine red in ethanol [26] proved to be a sensitive indicator, and the equivalence point was confirmed potentiometrically. The strength of the perchloric acid solution was checked before each run in order to avoid the effect of fluctuations in room temperature. Reactions were followed up to about 50% completion, this limit being determined by darkening of solutions in the case of lanosteryl toluene-*p*-sulphonate which reduced the sensitivity of the titrimetric end-point.

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[26] Highuchi, Feldman, and Rehm, *Analyt. Chem.*, 1956, **28**, 1120.

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646. *Chemical and Physical Properties of Some Sydnones.*

By D. Ll. HAMMICK and DENYS J. VOADEN.

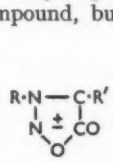
Some condensed-ring and related sydnones have been prepared, and their physical properties compared with those of the simpler derivatives.

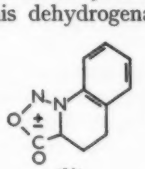
MANY mono- and di-substituted derivatives of sydnone (I; R = R′ = H) have now been recorded, and several of their general chemical reactions have been described.[1,2] In the present investigation, the chemical and physical properties of condensed-ring [3,4] and other sydnones [4] are compared with those previously known.

3′,4′-Dihydroquinolino[1′,2′-3,4]sydnone (II; " dihydronaphthosydnone " [3]) has been made from 1,2,3,4-tetrahydro-1-nitrosoquinaldinic acid and acetic anhydride [3] or trifluoroacetic anhydride. The action of thionyl chloride and pyridine on a dioxan solution of the nitroso-acid gave a purple oil, however, and not the expected sydnone.[5]

The dihydroquinolinosydnone (II) was hydrolysed by dilute alkali and by dilute mineral acid [3] in the manner general for sydnones.

Dehydrogenation of the sydnone (II) at the 3′,4′ positions should give the fully aromatic compound, but this dehydrogenation could not be achieved, either catalytically with


(I)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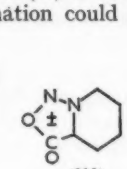
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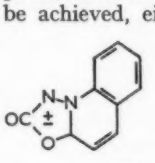
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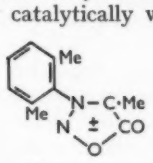
(V)

palladium on carbon alone, or in a solvent with ethyl cinnamate as hydrogen acceptor,[6] or chemically with sulphur, selenium dioxide, *N*-bromosuccinimide, or tetrachloro- or tetramethyl-*p*-benzoquinone.

Further, it was not possible to remove the hydrogen atoms at an earlier stage of the

[1] Eade and Earl, *J.*, 1946, 591.
[2] Baker and Ollis, *Quart. Rev.*, 1957, **11**, 15.
[3] Hammick, Roe, and Voaden, *Chem. and Ind.*, 1954, 251.
[4] Hammick and Voaden, *Chem. and Ind.*, 1956, 739.
[5] Cf. Baker, Ollis, and Poole, *J.*, 1950, 1543.
[6] Braude, Linstead, and Mitchell, *J.*, 1954, 3578.

XUM

synthesis, as tetrahydronitrosoquinaldinic acid was decomposed on reaction with *p*-benzoquinone in boiling tetrahydrofuran.

Kruger [7] has also described the sydnone (II), as well as the less easily accessible isomer derived from isoquinaldinic acid.

N-Nitrosopipecolic acid,[8] now isolated as a stable solid, readily gave 1′,2′,3′,4′-tetrahydropyridino[1′,2′-3,4]sydnone (III) on dehydration. This second condensed-ring sydnone possesses the ultraviolet spectrum of a typical alkylsydnone, and like 3-methylsydnone is soluble in cold water. It could not be dehydrogenated.

As sydnones unsubstituted at position 3 would rearrange to the isomeric 1,2,3-oxadiazol-5-ones [9] it seems that the simplest sydnone capable of existence is 3-methylsydnone [10] (I; R = Me, R′ = H), for which sarcosine is a readily available precursor. *N*-Nitrososarcosine can be dehydrated with acetic anhydride giving large, stable crystals of 3-methylsydnone.

When heated with benzylamine, some sydnones give the benzyl-amides of their parent nitroso-acids,[5] but it was not possible to effect this ring-opening with compounds (II) and (III), or with 4-methyl-3-*p*-tolylsydnone.

The ultraviolet spectra of simple sydnones possess a strong band (ε *ca.* 8000) at 290 mμ (alkyl) to 310 mμ (aryl). Compound (II), in which the sydnone nitrogen is linked to an aryl residue, would be expected to show this band near 310 mμ. However, the band which must be attributed to a sydnone ring actually lies at 340 mμ in 3′,4′-dihydroquinolino[1′,2′-3,4]sydnone. This is very near the values reported for the extensively conjugated 3,4-diarylsydnones—*e.g.*, 333 mμ [12] or 340 mμ [11] for 3,4-diphenylsydnone, and 338 mμ for 3,4-di-*p*-tolylsydnone.[13]

The combustion analysis, behaviour on hydrolysis, and presence of methylene bands in the infrared spectrum confirmed the identity of the dehydration product of tetrahydro-*N*-nitrosoquinaldinic acid, and it is suggested that the extended spectrum is due to enhanced conjugation permitted by molecular geometry.

Dipole-moment studies have shown that the moment of the sydnone ring is coplanar (at least within a small angle) with the phenyl–nitrogen link in 3-phenylsydnone, and that there is evidence for inter-ring resonance in such arylsydnones.[14] Crystallographic investigation shows that solid arylsydnones are " almost coplanar," [15] but presumably there is a certain amount of free rotation of the rings in 3-phenylsydnone. However, models indicated that the ethylene bridge, by forming an extra ring, holds the three rings of compound (II) in a coplanar configuration. From the present evidence, we can deduce that the molecule of the sydnone (II) is somewhat more planar than that of 3-phenylsydnone, and therefore that conjugation *via* the C–N link would be increased. The general form of the phenylsydnone spectrum is retained in that of the isosteric and isoelectronic 3-3′-pyridylsydnone, which is similar in most respects.[16]

The extended ultraviolet spectrum of 3′,4′-dihydroquinolino[1′,2′-3,4]sydnone (II) possesses three maxima—at 240, 260, and 340 mμ, and the mesoionic compound (IV), which has a close structural similarity, exhibits a spectrum of very similar general appearance with maxima at 226, 270, and 325 mμ.[17] However, one must note that compound (IV) possesses a double bond in the interannular bridge; a comparison of the spectrum of (II) with those of (IV) and its reduction product, if accessible, would be valuable.

[7] Kruger, *Chem. and Ind.*, 1954, 465.
[8] Willstätter, *Ber.*, 1896, **29**, 390.
[9] Baker and Ollis, *Quart. Rev.*, 1957, **11**, 21.
[10] Brookes and Walker, *J.*, 1957, 4416.
[11] Earl, Le Fèvre, and Wilson, *J.*, 1949, S105.
[12] Baker, Ollis, and Poole, *J.*, 1949, 311.
[13] Personal communication from Dr. Ollis.
[14] Hill and Sutton, *J.*, 1949, 746.
[15] Schmidt, *Bull. Res. Council Israel*, 1951, **1**, 121.
[16] Spectral data by courtesy of Prof. Hunsberger.
[17] Hoegerle, *Helv. Chim. Acta*, 1958, **41**, 553.

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The ultraviolet spectrum of *m*-tolylsydnone did not differ markedly from those of phenylsydnone and pyridylsydnone, as might be expected from the position of the small substituent. However, the presence of *ortho*-substituents in the phenyl ring, or of groups

Ultraviolet spectrophotometric data (mμ) for sydnones.

Sydnone	$\lambda_{max.}$	$\varepsilon_{max.}$	$\lambda_{min.}$	$\varepsilon_{min.}$	Sydnone	$\lambda_{max.}$	$\varepsilon_{max.}$	$\lambda_{min.}$	$\varepsilon_{min.}$
3-Methyl-	290	6600	225	170	Dihydroquinolino-	240	10,000	230	8250
3-Butyl-	289·5	6450	225	800		260	10,200	250	9650
3-Hexyl-	290·5	4950	242	500		340	5400	305	2450
Tetrahydropyridino-	295	9100	240	260	3-*o*-Tolyl-	300	6500	255	2100
3-Phenyl-	235	10,000	285	4250	3-*o*-Ethylphenyl-...	225 *	4250	255	2050
	255 *	7600				298·5	6500		
	310	5650			4-Ethyl-3-phenyl-	307	6200	265	1450
3-3′-Pyridyl-	236	10,000	258	7100	4-Methyl-3-*o*-tolyl-	235 *	3400	255	2050
	265	7300	295·5	4050		302·5	9550		
	312·5	4450			4-Methyl-3-*p*-tolyl-	240	6200	225	4900
3-*m*-Tolyl-	223	8800	219	8700		307	6600	275	2750
	253 *	6000	285·5	4000	4-Methyl-3-xylyl-	305	7800	250	1250
	310	4700							

* Inflexion.

replacing hydrogen at position 4 of the sydnone ring, modifies more or less profoundly the spectra in the 240—260 mμ region.

The effects of *ortho*-substitution on the ultraviolet spectra of biphenyls are now well known.[18] Qualitatively, similar effects, especially the steric resistance to interannular conjugation, are observed for the substituted 3-phenylsydnones.

A single methyl group immediately creates a pronounced minimum at 255 mμ in 3-*o*-tolylsydnone; the spectra of 3-*o*-ethylphenyl-, 4-ethyl-3-phenyl-, and 4-methyl-3-*o*-tolyl-sydnone are also very similar. Flexing of the ethyl groups may cause them to show no more steric effect than the methyl substituent.

4-Methyl-3-*p*-tolylsydnone possesses a maximum at 240 mμ, which may be related to a red shift which is favoured by *para*-substituents in benzene derivatives;[19] the sydnone-ring peak is 4 mμ further towards longer wavelength than in the *ortho*-isomer.

However, when the molecule is made more crowded by substitution in both *ortho*-positions, rotation and resonance must be much more hindered, and in the trisubstituted 4-methyl-3-(2,6-dimethylphenyl)sydnone (V), the ultraviolet spectrum begins to resemble that of an alkylsydnone, such as 3-n-butylsydnone.[16] The sydnone peak is conspicuous and in a normal position, but the minimum at 250 mμ is very weak.

The simple alkylsydnone spectrum is of course shown by 3-methylsydnone, 3-hexylsydnone,[16] and the tetrahydropyridinosydnone (III), and is of the form earlier reported for 3-benzylsydnone.[11]

The half-wave potentials for polarographic reduction of these sydnones are in accordance with the suggested steric effects, and will be discussed in relation to the spectra in a separate publication.[20]

Experimental

All (capillary) m. p.s are corrected unless otherwise stated.

3′,4′-Dihydroquinolino[1′,2′-3,4]*sydnone*.[3,7]—(*a*) A solution of 1,2,3,4-tetrahydro-1-nitroso-quinaldinic acid (2 g.) in acetic anhydride (20 ml.) was left for 6 days in the dark, then poured into dilute ammonia and worked up, giving the dihydroquinolinosydnone (1·19 g., 66%), m. p. 146°, and unchanged nitroso-acid (0·58 g.).

[18] See, *e.g.*, Beaven, in Gray (Ed.), "Steric Effects in Conjugated Systems," Butterworth, London, 1958, Ch. 3.

[19] Gillam and Stern, "An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," 2nd Edn., Arnold, London, 1957, p. 143.

[20] Zuman and Voaden, to be published; cf. Zuman, *Acta Chim. Acad. Sci. Hung.*, 1959, **18**, 143.

(*b*) Tetrahydronitrosoquinaldinic acid (1·4 g.), stirred in dry ether (25 ml.) at −10°, was treated with trifluoroacetic anhydride (1·5 g.). The suspension, poured into 3N-ammonia (16 ml.) at room temperature, gave the dihydroquinolinosydnone (0·75 g.; 59%); m. p. 145—145·5°, and unchanged nitroso-acid (0·42 g.).

The sydnone was stable to *ca.* 180°. A mull in paraffin showed an infrared C=O band at 5·80μ; a mull in bromonaphthalene showed a CH_2 band at 3·40μ.

Quinaldinic Acid Trifluoroacetate.—Quinaldinic acid (1·25 g.) in chloroform (25 ml.) at 45° was treated with trifluoroacetic acid (1 ml.). The white precipitate of *quinaldinic acid trifluoroacetate* (2·02 g.; 91%), m. p. 165—166°, crystallised as needles from acetone (Found: C, 50·1; H, 5·4. $C_{12}H_8NO_4F_3$ requires C, 50·2; H, 4·9%).

N-*Nitrosopipecolic Acid.*—Sodium nitrite (11·5 g.) solution was slowly added beneath the surface of stirred aqueous pipecolic acid hydrochloride (30 g.), and the liquid was extracted with ether for 40 hr. After removal of solvent, *N*-nitrosopipecolic acid (14·6 g.; 51%) remained as a viscous yellow oil, which solidified to prisms, m. p. 95—97°, after being dried *in vacuo* (P_2O_5). After being thoroughly drained, and washed with a little warm benzene, the nitroso-acid had m. p. 99° (decomp.) (Found: C, 45·4; H, 6·2; N, 17·8. Calc. for $C_6H_{10}N_2O_3$: C, 45·6; H, 6·4; N, 17·7%).

Mixed aqueous solutions of *N*-nitrosopipecolic acid and cupric sulphate slowly (2—3 months) deposited rosettes of bright green needles of the *monohydrated cupric salt* (Found: C, 36·5, 36·3; H, 5·4, 5·5; N, 13·7. $C_{12}H_{20}CuN_4O_7$ requires C, 36·4; H, 5·1; N, 14·2%).

1′,2′,3′,4′-*Tetrahydropyridino*[1′,2′-3,4]*sydnone.*—*N*-Nitrosopipecolic acid (13 g.), warmed with acetic anhydride (30 ml.), left 6 days in the dark, filtered, and evaporated *in vacuo* at 60°, gave a mass of white needles in brown tar (11·4 g.). This was stirred with light petroleum, as much as possible of the tar drained away, and recrystallised twice from ethyl acetate (41% overall recovery), giving a pure, Liebermann-negative *pyridinosydnone*, m. p. 104·5° [Found: C, 51·5; H, 5·6; N, 19·6, 20·2%; *M* (Rast), 162. $C_6H_8N_2O_2$ requires C, 51·4; H, 5·8; N, 20·0%; *M*, 140].

This sydnone began to decompose above 235°. In paraffin mull λ_{CO} was at 5·80 μ.

o-*Ethylanilinoacetic Acid.*—*o*-Ethylaniline (4 g.) and chloroacetic acid (2 g.) were boiled under reflux for 2½ hr. with water (25 ml.). After filtration, the solution rapidly deposited o-*ethylanilinoacetic acid* (1·85 g., 49%) as small needles, m. p. 147·5° not raised by further crystallisation (Found: C, 67·2; H, 7·1; N, 8·0. $C_{10}H_{13}NO_2$ requires C, 67·0; H, 7·3; N, 7·8%).

Preparation of N-*Nitroso-acids.*—These intermediates were all obtained by dissolving the appropriate imino-acid in N-hydrochloric acid and adding the calculated quantity of sodium nitrite solution with cooling. Initially, the products were often oily but they slowly solidified. They all gave a strong Liebermann test.

The following were thus obtained: o-*ethyl*-N-*nitrosoanilinoacetic acid*, m. p. 64° (Found: C, 57·4; H, 5·8. $C_{10}H_{12}N_2O_3$ requires C, 57·7; H, 5·8%); α-N-*nitrosoanilinobutyric acid* (98%) (from α-anilinobutyric acid [21]), m. p. 90—90·5° (decomp.) (from ether–light petroleum) (Found: N, 13·8. $C_{10}H_{12}N_2O_3$ requires N, 13·5%); N-*nitroso*-o-*toluidinoacetic acid* (69%) (from *m*-toluidinoacetic acid [22]), m. p. 80·5—82·5° (Found: N, 14·4. $C_9H_{10}N_2O_3$ requires N, 14·4%); α-(N-*nitroso*-o-*toluidino*)*propionic acid* (89%) (from α-*o*-toluidinopropionic acid [23]), m. p. 93—95° (decomp.) (Found: C, 57·6; H, 5·9; N, 13·4. $C_{10}H_{12}N_2O_3$ requires C, 57·7; H, 5·8; N, 13·5%); α-(N-*nitroso*-p-*toluidino*)*propionic acid* (88%) (from α-*p*-toluidinopropionic acid [24]), m. p. 110° (decomp.) (as needles from benzene) (Found: C, 57·5; H, 5·9; N, 13·1%); and α-(2,6-*dimethyl*-N-*nitroso*)*propionic acid* by nitrosation of the solution from refluxing of 2,6-dimethylaniline and α-bromopropionic acid in water for 21 hr. (Found: N, 12·0. $C_{11}H_{14}N_2O_3$ requires N, 12·6%).

Preparation of Arylsydnones.—The appropriate *N*-nitroso-acid was dehydrated with acetic anhydride, sometimes for *ca.* 1 hr. at 100°, but more often by leaving the reactants for 1—3 days at room temperature, and then working them up with dilute ammonia. The following were obtained: 3-o-*ethylphenylsydnone*, small white needles, m. p. 69·5°, after two crystallisations

[21] Nastvogel, *Ber.*, 1889, **22**, 1794.
[22] A. Ehrlich, *Ber.*, 1882, **15**, 2011.
[23] Steppes, *J. prakt. Chem.*, 1900, **170**, 498.
[24] Steppes, *J. prakt. Chem.*, 1900, **170**, 495.

from water (Found: C, 63·1; H, 5·6. $C_{10}H_{10}N_2O_2$ requires C, 63·2; H, 5·3%), λ_{OO} 5·69 μ; *4-ethyl-3-phenylsydnone* (75% yield), m. p. 75°, λ_{OO} 5·78 μ, after 3 crystallisations from ether [Found: C, 63·6; H, 5·5; N, 14·4, 14·6%; *M* (Rast), 212. $C_{10}H_{10}N_2O_2$ requires C, 63·2; H, 5·3; N, 14·7%; *M*, 190]; *3-o-tolylsydnone* (74%), needles, m. p. 100°, λ_{OO} 5·69 μ, from boiling water (lit., m. p. 89°,[25] 96° [26]) (Found: C, 61·3; H, 4·4; N, 15·8. Calc. for $C_9H_8N_2O_2$: C, 61·4; H, 4·6; N, 15·9%); *3-m-tolyl compound* (61%), small white needles, m. p. 79° (Kofler), λ_{OO} 5·66 μ, after 3 recrystallisations from water (Found: C, 61·3; H, 4·8; N, 15·5%); *4-methyl-3-o-tolylsydnone* (90%), m. p. 72°, λ_{OO} 5·70 and 5·80 μ [Found: 63·2; H, 5·5; N, 14·6%; *M* (Rast), 170. $C_{10}H_{10}N_2O_2$ requires C, 63·2; H, 5·3; N, 14·7%; *M*, 190]; *4-methyl-3-p-tolylsydnone* (74%), prisms, m. p. 166·5°, λ_{OO} 5·67 and 5·76 μ after two recrystallisations from methanol [Found: C, 63·4; H, 5·3; N, 15·2%; *M* (Rast), 191]; *3-(2,6-dimethylphenyl-4-methylsydnone* (crude yield 55%), small prisms, m. p. 120·5—121°, λ_{OO} 5·71 and 5·79 μ, after three recrystallisations from water (Found: C, 65·0; H, 6·2; N, 13·5. $C_{11}H_{12}N_2O_2$ requires C, 64·7; H, 5·9; N, 13·7%).

Acid hydrolysis of an ethanolic solution of 4-methyl-3-*p*-tolylsydnone gave *p*-tolylhydrazine hydrochloride, m. p. 222° (decomp.) (lit.,[27] m. p. 222—235°).

α-m-*Toluidinopropiono*-m-*toluidide*.—*m*-Toluidine (20 g.), α-bromopropionic acid (11 g.), and water (100 ml.) were boiled overnight; after free amine and some resin had been removed, and the liquid refrigerated, white crystals slowly appeared, which had m. p. 115° after two recrystallisations from aqueous methanol. These appeared to be α-m-*toluidinopropiono*-m-*toluidide* (Found: C, 76·1; H, 7·3; N, 10·6, 10·7. $C_{17}H_{20}N_2O$ requires C, 76·1; H, 7·5; N, 10·4%). By nitrosating the filtrate from this amide, a very small amount of α-(*N*-nitroso-*m*-toluidino)propionic acid, m. p. 99·5° (decomp.), was obtained.

Ethyl α-(2,6-*Dimethylanilino*)*propionate*.—2,6-Dimethylaniline (10 g.) and ethyl α-bromopropionate (5 g.) in benzene (25 ml.) were refluxed 96 hr. Crystals of 2,6-*dimethylanilinium bromide* (3·26 g.; 58%) (Found: C, 47·1; H, 6·2. $C_8H_{12}BrN$ requires C, 47·5; H, 6·0%) were removed, and the filtrate fractionated. *Ethyl* α-(2,6-*dimethylanilino*)*propionate* (2·26 g., 37%) after two distillations had b. p. 146—148°/20—21 mm., 166°/45 mm. (Found: C, 70·2; H, 8·6; N, 6·6. $C_{13}H_{19}NO_2$ requires C, 70·6; H, 8·7; N, 6·3%).

2,6-*Dimethylanilinium bromide monohydrate*, forming laths from dilute hydrobromic acid, had m. p. 232° (slight decomp., loss of water at *ca.* 100°) (Found: Br, 36·3. $C_8H_{12}BrN,H_2O$ requires Br, 36·3%).

N-Nitrososarcosine.—Commercial sarcosine solution (450 ml.; *ca.* 12% w/v) was made alkaline with sodium hydroxide, boiled to expel methylamine, and acidified with 10N-hydrochloric acid. After removal of sodium chloride, the filtrate was treated with sodium nitrite (37 g.) solution, and extracted for 36 hr. with ether. This gave *N*-nitrososarcosine (64 g., 88%) as a viscous yellow oil.

The acid exploded (mildly) on attempted distillation at 160°/0·18 mm. Another sample, heated for a time at 40°/15 mm., set on cooling to a yellow slush, which was drained and crystallised thrice from chloroform. This gave solid *N*-nitrososarcosine with m. p. 73—74° (Found: C, 30·8; H, 5·2; N, 23·9. Calc. for $C_3H_6N_2O_3$: C, 30·5; H, 5·2; N, 23·8%).

3-Methylsydnone.—*N*-Nitrososarcosine (38 g.) in acetic anhydride (120 ml.), warmed for a few minutes on a steam-bath, became very hot. The mixture was left for 3 days and the excess of anhydride was then removed *in vacuo*. Two distillations of the residue gave a liquid, b. p. 147—148°/0·15 mm., which solidified, m. p. 35—36° (9·8 g.; 31%). The pure, Liebermann-negative sydnone, obtained after two further distillations, had b. p. 125—128°/0·12 mm. (lit.,[10] b. p. 140—142°/0·2 mm.), m. p. 36°, λ_{OO} at 5·82 μ (film) (Found: C, 36·1; H, 4·3; N, 28·2. Calc. for $C_3H_4N_2O_2$: C, 36·0; H, 4·0; N, 28·0%).

Methylhydrazine from 3-Methylsydnone.—3-Methylsydnone (4 g.) and 10N-hydrochloric acid (8 ml.) were heated for 4 hr. at 100°. On addition of a further 3 ml. of acid, and refrigeration overnight, glistening white platelets of *methylhydrazine sesquihydrochloride sesquihydrate* (3·1 g.; 62%) were obtained, with m. p. 118° (sealed tube, lost water from 60°) (Found: C, 9·8; H, 7·2. $CH_6N_2,1\frac{1}{2}HCl,1\frac{1}{2}H_2O$ requires C, 9·5; H, 7·2%). When dried *in vacuo* (P_2O_5) the hygroscopic *methylhydrazine sesquihydrochloride* (Found: C, 11·5; H, 7·5; Cl, 54·0; loss, 21·8. $CH_6N_2,1\frac{1}{2}HCl$ requires C, 11·9; H, 7·5; Cl, 53·0; loss, 19·2%) was obtained.

[25] Hadaček and Švehla, *Publ. Fac. Sci. Univ. Masaryk*, 1954, **357**, 257.
[26] Hashimoto and Ohta, *Bull. Chem. Soc., Japan*, 1958, **31**, 1049.
[27] Hunsberger *et al.*, *J. Org. Chem.*, 1956, **21**, 396.

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647. *Methyl Glucosides as Transfer Agents in Polymerisation of Acrylonitrile and Styrene.*

By G. MACHELL and G. N. RICHARDS.

Methyl 6-deoxy-6-dipropylamino-β-D-glucopyranoside and methyl 6-deoxy-6-mercapto-α-D-glucopyranoside have been synthesised. The transfer constants of these and other glucoside derivatives have been determined in polymerisation of acrylonitrile and styrene. The results are in accordance with earlier results on the use of tertiary amines and thiols as transfer agents. The use of the transfer reaction in graft polymerisation on cellulose derivatives is discussed.

THE transfer reaction in free-radical addition polymerisation may be summarised as:

$$R\cdot + T \longrightarrow P + T\cdot$$
$$T\cdot + M \longrightarrow T\text{-}M\cdot$$

where R· is a growing polymer radical, P a " dead " polymer molecule, M the monomer, and T the transfer agent. The new radical T· is usually capable of initiating polymerisation as shown. When T represents a preformed polymer, transfer at a modified end-group has been used to prepare block copolymers,[1] and if transfer occurs at points along the preformed polymer the transfer reaction initiates graft polymerisation. In order to consider the possibility of using cellulose derivatives as transfer agents to produce graft copolymers in this way it was necessary to know the relative transfer efficiency of various groupings which could be attached to the cellulose molecule. The transfer constants of a range of glucoside derivatives have therefore been determined. Three of those studied were new compounds.

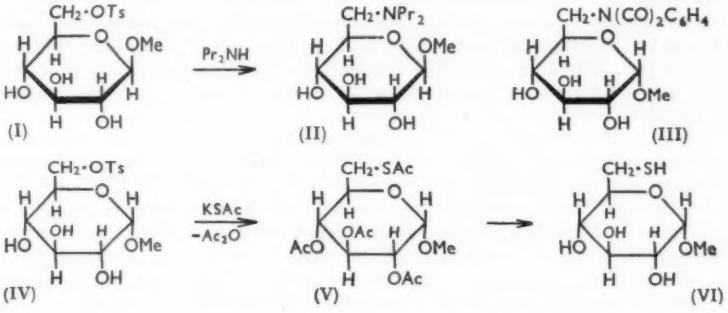
Methyl 6-deoxy-6-dipropylamino-β-D-glucopyranoside (II) was prepared by heating methyl 6-*O*-toluene-*p*-sulphonyl-β-D-glucopyranoside (I) with dipropylamine, reaction being analogous to that used by Freudenberg and Smeykal [2] to prepare a 6-deoxy-6-dimethylaminogalactose derivative. Methyl 6-deoxy-6-phthalimido-α-D-glucopyranoside (III) was similarly prepared by treatment of methyl 6-*O*-toluene-*p*-sulphonyl-α-D-glucopyranoside (IV) with potassium phthalimide.

Apart from 1-deoxy-1-mercapto-derivatives, the only deoxymercapto-derivative of an aldose or aldoside with a free thiol grouping so far isolated and properly characterised is the 6-deoxy-6-mercapto-D-glucose of Ohle *et al.*,[3] which was prepared by treatment of a 5,6-anhydro-sugar with hydrogen sulphide. Owen and his co-workers [4] have, however, prepared several thiols in the hexitol series and one of their methods has now been successfully employed in the glucoside series as follows. Methyl 6-*O*-toluene-*p*-sulphonyl-α-D-glucopyranoside (IV) was heated with potassium mercaptoacetate in acetone, yielding

[1] Bamford and White, *Trans. Faraday Soc.*, 1956, **52**, 716.
[2] Freudenberg and Smeykal, *Chem. Ber.*, 1926, **59**, 100.
[3] Ohle and Merten, *Chem. Ber.*, 1935, **68**, 2176.
[4] Creighton and Owen, *J.*, 1960, 1024 and earlier references.

methyl 6-acetylthio-6-deoxy-α-D-glucopyranoside which was then acetylated. The tetra-acetyl derivative (V) was then catalytically deacetylated to methyl 6-deoxy-6-mercapto-α-D-glucopyranoside (VI): the analysis and infrared spectrum were in agreement with this structure.

The transfer constants of compounds (II), (III), and (VI) and several other glucosides



were determined in the polymerisation of acrylonitrile in dimethylformamide solution with azodi-isobutyronitrile as catalyst and also in the uncatalysed bulk polymerisation of styrene. The results are summarised in Tables 1 and 2.

Experimental

Preparation of Methyl 6-Deoxy-6-dipropylamino-β-D-glucopyranoside (II).—Methyl β-D-glucopyranoside (20 g.) was converted by Compton's method [5] into methyl 2,3,4-tri-*O*-acetyl-6-*O*-toluene-*p*-sulphonyl-β-D-glucopyranoside (22·5 g.), m. p. 167—168°, $[\alpha]_D^{20}$ +6·5° (*c* 4 in chloroform), $[\alpha]_D^{20}$ +3° (*c* 2 in pyridine) {Helferich *et al.*[6] give m. p. 171°, $[\alpha]_D^{20}$ +33·1° (*c* 7 in pyridine)} (Found: C, 50·6; H, 5·5; OMe, 6·7. Calc. for $C_{20}H_{26}O_{11}S$: C, 50·6; H, 5·5; 1OMe, 6·5%). A portion (3·50 g.) of this product was suspended in dry methanol (100 ml.), and sodium methoxide (0·05 g.) in methanol (3 ml.) was added. Dissolution was complete after ½ hour's stirring and after a total of 18 hr. at room temperature *methyl 6-O-toluene-p-sulphonyl-β-D-glucoside* (2·25 g.) was isolated as a colourless syrup and dried at 40°/0·01 mm. over phosphoric oxide; it had $[\alpha]_D^{21}$ −11° (*c* 2 in ethanol) (Found: C, 48·5; H, 5·9. $C_{14}H_{20}O_8S$ requires C, 48·3; H, 5·8%).

The whole of the above product was heated with dipropylamine (5 ml.) at 100° for 18 hr. and then the unchanged amine was removed under reduced pressure. The residue was dissolved in water, the solution passed through a column of Amberlite resin IRA-400(OH) (15 ml.), and the effluent evaporated to a syrup which crystallised slowly. After recrystallisation from ethyl acetate the *methyl 6-deoxy-6-dipropylamino-β-D-glucopyranoside* (1·25 g.) had m. p. 117—118° and $[\alpha]_D^{26}$ −49·5° (*c* 2 in ethanol) (Found: C, 56·1; H, 9·6; N, 4·75%; equiv., 278. $C_{13}H_{27}NO_5$ requires C, 56·3; H, 9·8; N, 5·05%; equiv., 277).

Similar treatment of methyl 6-*O*-toluene-*p*-sulphonyl-α-D-glucopyranoside gave a syrup.

Preparation of Methyl 6-Deoxy-6-phthalimido-α-D-glucopyranoside (III).—Methyl 6-*O*-toluene-*p*-sulphonyl-α-D-glucopyranoside (3·0 g.), prepared as described by Cramer *et al.*,[7] and potassium phthalimide (2·0 g.) were suspended in dimethylformamide (40 ml.) and heated at *ca.* 100° for 24 hr., during which the solids slowly dissolved, and then at 110—115° for a further 4 hr. After cooling, the solution was poured into water, and a small amount of phthalimide was removed. The filtrate was deionised with Amberlite resins IR-120(H) (15 ml.) and IRA-400 (carbonate) (25 ml.) and evaporated to dryness. Crystallisation of the resulting syrup from methanol–acetone and then ethyl acetate–ethanol afforded *methyl 6-deoxy-6-phthalimido-α-D-glucopyranoside* (0·83 g., 30%), m. p. 167—169°. When further recrystallised from ethanol this

[5] Compton, *J. Amer. Chem. Soc.*, 1938, **60**, 395.
[6] Helferich, Bredereck, and Schneidmüller, *Annalen*, 1927, **458**, 111.
[7] Cramer, Otterbach, and Springmann, *Chem. Ber.*, 1959, **92**, 384.

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material had m. p. 171—173°, $[\alpha]_D^{22}$ +86·5° (*c* 2 in H_2O) (Found: C, 55·5; H, 5·5; N, 4·2. $C_{15}H_{17}NO_7$ requires C, 55·7; H, 5·3; N, 4·3%).

Preparation of Methyl 6-*Deoxy*-6-*thio*-α-D-*glucopyranoside* (VI).—A solution of methyl 6-*O*-toluene-*p*-sulphonyl-α-D-glucopyranoside [7] (IV) (10·0 g.) and potassium mercaptoacetate (4·0 g.) in acetone (400 ml.) was boiled under reflux for 7 hr., then cooled, and the crystalline potassium toluene-*p*-sulphonate filtered off (5·67 g., 94%). The filtrate was evaporated to a yellow viscous syrup (7·9 g.) which was treated with acetic anhydride (50 ml.) in dry pyridine (100 ml.) at room temperature for 20 hr. The resulting solution was poured into water and the *methyl* 2,3,4-*tri*-O-*acetyl*-6-*acetylthio*-6-*deoxy*-α-D-*glucopyranoside* (V) extracted with chloroform and distilled at 165—170°/0·02 mm. The distillate (6·4 g.) was a pale yellow glass, n_D^{20} 1·4792, $[\alpha]_D^{20}$ +118° (*c* 1 in chloroform) (Found: C, 48·0; H, 6·2; S, 8·5. $C_{15}H_{22}O_9S$ requires C, 47·6; H, 5·9; S, 8·5%).

The acetate (0·92 g.) was kept in dry methanol (20 ml.) containing sodium methoxide (0·05 g.) at room temperature for 20 hr. The solution was then evaporated to dryness, and the residue dissolved in water, deionised with Amberlite resins IR-120(H) and IRA-400 (carbonate), and again evaporated to a colourless syrup (0·45 g.), which was dried at 40°/0·02 mm. over phosphoric oxide. The *methyl* 6-*deoxy*-6-*thio*-α-D-*glucopyranoside* (VI), which was not further purified, had $[\alpha]_D^{20}$ +181° (*c* 0·5 in ethanol) (Found: C, 40·2; H, 7·0; S, 14·6. $C_7H_{14}O_5S$ requires C, 40·0; H, 6·7; S, 15·2%). The infrared spectrum was almost identical with that of methyl α-D-glucopyranoside, except for the weak S–H absorption at 2550 cm.$^{-1}$. In addition the peak at 845 cm.$^{-1}$ for the *O*-derivative was shifted to 875 cm.$^{-1}$ for the thiol and the 1250 cm.$^{-1}$ absorption was intensified.

Purification of Materials.—The purification of several of the model compounds has been described above; the remainder were purified according to the previously published methods. All of the compounds used had the appropriate elemental analyses. Acrylonitrile was purified as described by Bamford and Jenkins [8] and kept in the dark at 0°. Styrene was washed with 5N-sodium hydroxide and then with water, dried ($CaCl_2$), fractionally distilled under nitrogen at *ca.* 20 mm., and used immediately. Azodi-isobutyronitrile was twice recrystallised from toluene at <40°. Dimethylformamide was kept over phosphoric oxide at room temperature for several hours, then decanted and fractionally distilled at 1 atm. Dioxan was boiled under reflux with sodium for 4 hr., then fractionally distilled at 1 atm. from sodium just before use.

Polymerisation of Acrylonitrile.—The transfer agent (0·5—2 g.) was weighed into a glass ampoule, and acrylonitrile (10·0 ml.) and a solution of azodi-isobutyronitrile (0·020 g.) in dimethylformamide (40 ml.) added. The mixture was frozen, degassed at 0·01 mm., allowed to melt, refrozen, and again degassed at 0·01 mm. before sealing. The tubes were heated in a bath at 60° ± 0·1° for 90 min. with occasional shaking and the solution then added to methanol (150 ml.) with vigorous stirring. The precipitate was filtered off, washed with methanol, and dried at 40°/20 mm. over calcium chloride (yield 0·5—0·6 g.).

Polymerisation of Styrene.—The transfer agent (0·5—2 g.) and styrene (10·0 ml.) were degassed as above and heated in a bath at 100° ± 0·5° for 1 hr. with occasional shaking, and the polystyrene (0·1 g.) was isolated as described for polyacrylonitrile. In this case the polymer was redissolved in toluene and reprecipitated with methanol (5 vol.) before drying. In the experiments with the thiol (VI), a solution of it (0·02 g.) in dioxan (8·0 ml.) and styrene (8·0 ml.) was polymerised at 100° for 4 hr. and the polystyrene (0·2 g.) isolated as above.

Determination of Transfer Constants.—" Specific viscosities " of polyacrylonitrile and polystyrene were determined in a capillary viscometer at 25° in dimethylformamide and toluene solution respectively. The limiting viscosity number,[9] $[\eta]$, was determined from the Schulz–Sing relation,[10] $c[\eta] = \eta_{sp}/(1 + 0{\cdot}28\eta_{sp})$, where c is the concentration of polymer expressed in g./ml., and $\eta_{sp} = (t - t_0)/t_0$, with t and t_0 the viscometer flow-times.

The molecular weights were calculated from the Houwink equation ($[\eta] = K\bar{M}^{\alpha}$), the following constants being used: for polyacrylonitrile,[11] $K = 4{\cdot}72 \times 10^{-3}$, $\alpha = 0{\cdot}733$; for polystyrene,[12] $K = 1{\cdot}74 \times 10^{-2}$, $\alpha = 0{\cdot}714$.

The use of a single set of parameters for varying concentrations of transfer agents introduces

[8] Bamford and Jenkins, *Proc. Roy. Soc.*, 1953, *A*, **216**, 515.
[9] International Union of Pure and Applied Chemistry, *J. Polymer Sci.*, 1952, **8**, 257.
[10] Schulz and Sing, *J. prakt. Chem.*, 1943, **161**, 161.
[11] Bamford, Jenkins, Johnston, and White, *Trans. Faraday Soc.*, 1959, **55**, 168.
[12] Gregg and Mayo, *J. Amer. Chem. Soc.*, 1948, **70**, 2373.

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errors in the determination of molecular weight from viscosity (cf. ref. 11), but since we are concerned at the present stage with relative transfer efficiencies, with a wide range of values, this procedure is considered adequate.

The transfer constants were calculated from the Mayo equation,[13]

$$\frac{1}{\bar{P}} - \frac{1}{P_0} = C\frac{[S]}{[M]}$$

where P and P_0 are, respectively, the degree of polymerisation of polymer prepared with and without transfer agent, [S] and [M] are concentrations of transfer agent and monomer, and C is the transfer constant. The adherence to the Mayo equation is shown by the linear dependence of $1/P$ with [S]/[M], in the case of methyl 6-deoxy-6-dipropylamino-β-D-glucopyranoside (II) with acrylonitrile (Table 1).

The results are shown in Tables 1 and 2.

TABLE 1. *Polymerisation of acrylonitrile at 60° in dimethylformamide with azodi-isobutyronitrile (0·4 g./l.) as catalyst.*

Transfer agent	10^2[S]/[M]	$\bar{P}$	10^2C	Transfer agent	10^2[S]/[M]	$\bar{P}$	10^2C
	0	708	0	Me 6-*O*-triphenylmethyl-α-D-glucoside	3·55	582	0·9
Me α-D-glucoside	6·70	659	0·2		3·60	586	0·8
	3·90	687	0·1	Me 2,3-di-*O*-benzyl-α-D-glucoside	2·66	596	1·0
Me β-D-glucoside	2·78	681	0·2		1·51	649	0·9
Me 6-*O*-toluene-*p*-sulphonyl-α-D-glucoside	2·19	703	<0·1	Me 6-deoxy-6-dipropylamino-β-D-glucoside (V)	1·43	337	10·9
	1·38	698	<0·1		1·19	366	11·1
Me 2,3,4,6-tetra-*O*-acetyl-α-D-glucoside	4·19	666	0·25		1·02	388	11·5
	2·03	681	0·3		0·595	474	11·8
Me 6-deoxy-6-iodo-α-D-glucoside	4·20	622	0·5	Me 6-deoxy-6-mercapto-α-D-glucoside (V)	0·13	638	12
	2·48	646	0·6		0·11	634	14
Me 6-deoxy-6-phthalimido-α-D-glucoside	1·89	666	0·5				
	1·10	685	0·5				

TABLE 2. *Bulk polymerisation of styrene at 100°.*

Transfer agent	10^2[S]/[M]	$\bar{P}$	10^2C	Transfer agent	10^2[S]/[M]	$\bar{P}$	10^2C
	0	5485	0	Me 6-deoxy-6-dipropylamino-β-D-glucoside (II)	1·93	4420	0·22
Dioxan	134·0	3350	0·009				
	134·0	3480	0·008	Me 2,3,4-tri-*O*-acetyl-6-deoxy-6-iodo-α-D-glucoside	4·02	2600	0·50
Me 2,3,4,6-tetra-*O*-acetyl-α-D-glucoside	4·53	5260	0·02		2·69	3200	0·49
	2·99	5260	0·025	Me 2,3-di-*O*-benzyl-α-D-glucoside	2·91	2765	0·615
Me 6-*O*-toluene-*p*-sulphonyl-α-D-glucoside (IV)	2·22	5380	0·02		2·18	3105	0·64
Me 6-*O*-triphenylmethyl-α-D-glucoside	1·80	4540	0·21	*Me 6-deoxy-6-thio-α-D-glucoside (VI)	0·164	106	557·0
	1·39	4730	0·21		0·149	118	546·0

* In 1 : 1 v/v dioxan–styrene solution (P_0 = 3415).

DISCUSSION

The results in Table 1 show that the acetal, *O*-acetyl, *O*-toluene-*p*-sulphonyl, and hydroxyl groupings in methyl glucosides are very inefficient transfer agents for polyacrylonitrile radicals. The 6-deoxy-6-iodoglucoside shows a somewhat greater transfer efficiency, in accordance with the general trend observed with other halides.[14] The higher transfer constant of the di-*O*-benzyl ether probably reflects the known susceptibility of the benzyl CH_2 grouping to radical attack.[15] The 6-*O*-triphenylmethyl ether and the phthalimido-group are evidently also rather susceptible to attack by the polyacrylonitrile radical.[16]

[13] Mayo, *J. Amer. Chem. Soc.*, 1943, **65**, 2324.
[14] *E.g.*, Palit and Das, *Proc. Roy. Soc.*, 1954, *A*, **226**, 82.
[15] Cf. Walling, "Free Radicals in Solution," Wiley and Sons, Inc., New York, 1957, p. 402; Debiais, Niclause, and Letort, *J. Chim. phys.*, 1959, **56**, 41.
[16] Cf. Gregg and Mayo, *Discuss. Faraday Soc.*, 1947, **2**, 328.

Methyl 6-deoxy-6-dipropylamino-β-D-glucopyranoside (II), however, shows a very much higher transfer constant in reaction with acrylonitrile and this is almost certainly due to the resonance stabilisation of the transition-state complex between the tertiary amino-group and the polyacrylonitrile radical, which has been postulated for simple amines by Bamford and White.[1] The results of these authors on a series of amines suggest that compound (II) should be the most effective glucoside transfer agent of its (amine) type in acrylonitrile polymerisation. The thiol grouping, as in (VI), is also very effective in transfer with the polyacrylonitrile radical, but this group reacts even more readily with polystyrene radicals.

The results of Table 2 show that the acetal, *O*-acetyl, *O*-toluene-*p*-sulphonyl, and hydroxyl-groupings in the glucosides are relatively unreactive with polystyrene radicals, but the deoxyiodo- and the *O*-triphenylmethyl and *O*-benzyl ether groups show moderate reactivity, as in the reaction with polyacrylonitrile radicals. The tertiary amino-derivative (II), however, fails to show the superior reactivity which was observed with acrylonitrile (Table 1) and this is in accordance with Bamford and White's postulate [1] that the tertiary amines react most readily with radicals which are powerful electron-acceptors. The thiol (VI) has a very high transfer constant with polystyrene radicals and this is in accord with general observations on simple thiols.[17] Walling has suggested [18] that the effect is due to electron-donation to the thiol by the polymeric radical in the transition-state complex.

It is expected that these results for model compounds will be used to derive the relative reactivities of, for example, cellulose derivatives, to graft polymerisation by the transfer reaction. This type of model-compound approach has previously been used by Schonfield and Waltcher [19] with a brominated polyester and by Graham and his co-workers [20] with a thiol derivative of a polyvinyl, and the transfer constants of the polymers were similar to those of an analogous model. Our results suggest that either a deoxydipropylamino- or a deoxythio-cellulose derivative should readily form a graft copolymer with polyacrylonitrile on transfer reaction with polyacrylonitrile radicals, and that the deoxythio-derivative should be particularly efficient in similar grafting with styrene. The results also indicate that very little true transfer will occur when acrylonitrile or styrene is polymerised in presence of cellulose itself or any other common hydroxylated polymer.

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[17] Gregg, Alderman, and Mayo, *J. Amer. Chem. Soc.*, 1948, **70**, 3740; Dinaburg and Vansheidt, *J. Gen. Chem.* (*U.S.S.R.*), 1954, **24**, 840.
[18] Walling, *J. Amer. Chem. Soc.*, 1948, **70**, 2561.
[19] Schonfeld and Waltcher, *J. Polymer Sci.*, 1959, **35**, 536.
[20] Gluckman, Kampf, O'Brien, Fox, and Graham, *J. Polymer Sci.*, 1959, **37**, 411.

648. *Photochemical Transformations. Part XI.* The Photochemistry of Pentacyclic Triterpenoids with Diene Unsaturation in Ring C.*[1]

By R. L. Autrey, D. H. R. Barton, A. K. Ganguly, and W. H. Reusch.

Irradiation of methyl dehydroursolate acetate affords an isomeric triene, analogous to precalciferol, which isomerises thermally to a further triene comparable in its structure with calciferol itself. The generality of such cleavage is discussed in structural terms.

The photoisomerisation of steroidal 5,7-dienes (as I) is one of the most thoroughly studied of photochemical reactions.[2] It has been established that the initial photochemical act affords a triene (as II)[3] which subsequently isomerises purely thermally to the vitamin D type of triene (as III). These, and other aspects, of the photochemical behaviour of steroidal 5,7-dienes have been studied especially by Havinga and his colleagues.[4]

At the outset of the present investigations it seemed to us that the photochemical cleavage of a homoannular cyclohexadiene ring, such as that of (I) into (II), should be a general reaction, although according to Jeger, Redel, and Nowak[5] irradiation of dehydro-α-amyrin acetate (IV; R = Ac, R′ = Me) and of methyl dehydroursolate acetate (IV; R = Ac, R′ = CO_2Me) gave products that showed only terminal absorption at 220 mμ in the ultraviolet region and were therefore not the expected trienes (V; R = Ac, R′ = Me and CO_2Me, respectively). In fact, we quickly established that irradiation of methyl dehydroursolate acetate in boiling ether caused disappearance of the homoannular diene band near 280 mμ and appearance of a new band near 240 mμ which eventually reached an intensity of ε ~9000. Removal of the ether gave non-crystalline material with the same spectrum. Refluxing in ethanol solution without irradiation then led to the diminution and eventual disappearance of the 240 mμ band concomitant with the development of a new band at 261 mμ. Removal of the solvent at this stage then afforded a crystalline product shown in the sequel to have structure (VI; R = Ac, R′ = CO_2Me). For preparative purposes the process can be carried out in refluxing ethanol, irradiation being interrupted when the initial diene band has disappeared; the purely thermal isomerisation is subsequently allowed to proceed under reflux. Yields of approximately 75% can be attained.

The constitution of the triene (VI; R = Ac, R′ = CO_2Me) is based upon the following facts. The ultraviolet spectrum is consistent with a triene system,[6] and the infrared spectrum shows a band near 890 cm.$^{-1}$ assignable to (>C=CH_2). Ozonolysis of the triene gave formaldehyde, a crystalline dicarboxylic acid, and an oily keto-ester. The crystalline acid was shown to have structure (VIII; R = Ac, R′ = H) in the following way. Hydrolysis gave the hydroxy-dicarboxylic acid (VIII; R = R′ = H) which on methylation and benzoylation or 3,5-dinitrobenzoylation afforded the derivatives (VIII; R = acyl, R′ = Me). Authentic racemic benzoate dimethyl ester (VIII; R = Bz, R′ = Me) was readily prepared by oxidation of the synthetic keto-benzoate[7] (XI; R = Bz) with chromic acid to the acid (VIII; R = Bz, R′ = H), followed by methylation. Comparison of infrared spectra established identity. The neutral keto-ester, $[\alpha]_D$ −27°, was shown to have structure (IX; R = Me) by the following experiments. Vigorous alkaline hydrolysis

* Part X, *J.*, 1961, 1215.

[1] Preliminary account: Autrey, Barton, and Reusch, *Proc. Chem. Soc.*, 1959, 55.

[2] Fieser and Fieser, "Steroids," Reinhold Publ. Corpn., New York, 1959, pp. 90 *et seq.*

[3] Velluz, Petit, Michel, and Rousseau, *Compt. rend.*, 1948, **226**, 1287; Velluz, Petit, and Amiard, *Bull. Soc. chim. France*, 1948, 1115; Velluz, Amiard, and Petit, *ibid.*, 1949, 501.

[4] Rappoldt and Havinga, *Rec. Trav. chim.*, 1960, **79**, 369; and many earlier papers.

[5] Jeger, Redel, and Nowak, *Helv. Chim. Acta*, 1946, **29**, 1241.

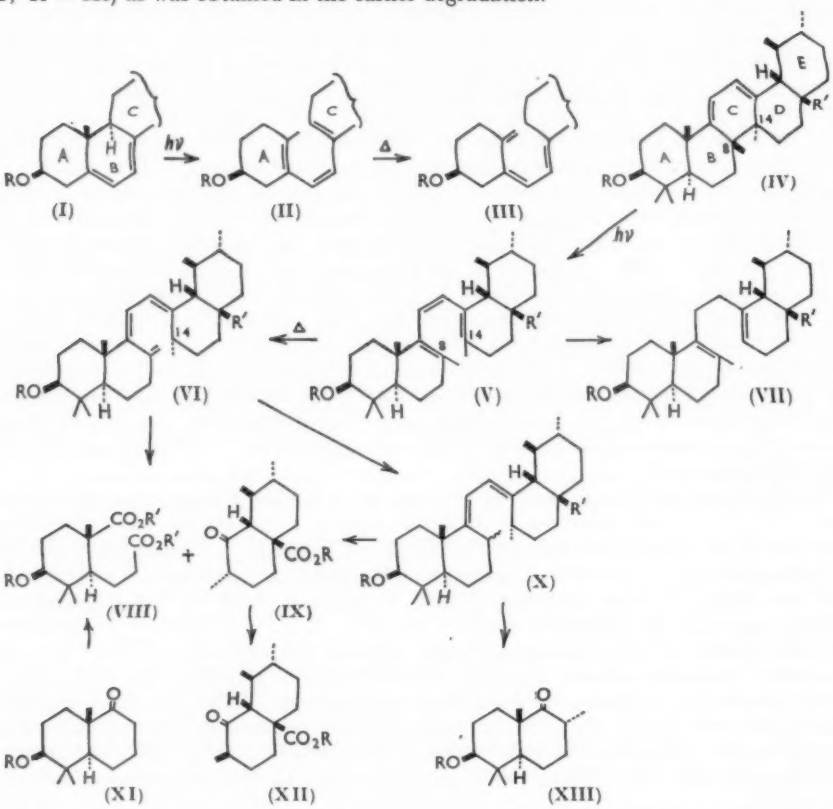
[6] Fieser and Fieser, *op. cit.*, pp. 15 *et seq.*

[7] Sondheimer and Elad, *J. Amer. Chem. Soc.*, 1958, **80**, 1967; see also Gaspert, Halsall, and Willis, *J.*, 1958, 624; Kalvoda and Loeffel, *Helv. Chim. Acta*, 1957, **40**, 2340.

XUM

furnished a crystalline keto-acid which must be (XII; R = H) because of its constitution and of the way in which it is derived. Remethylation of the acid gave a different methyl ester which had $[\alpha]_D$ −108°. Since the keto-acid has certainly been equilibrated by the hydrolytic conditions we assign the more stable equatorial configuration to the α-methyl group as already indicated in the formula. The original keto-ester must therefore have the opposite (α-)configuration, as written in the formula (IX; R = Me). Isomerisation of the *cis*- to *trans*-decalone is, of course, excluded by the cogent arguments of Corey and Ursprung.[8]

Further proof of the constitution of the triene (VI; R = Ac, R′ = CO_2Me) was secured in the following way. Selective hydrogenation of the triene gave a dihydro-derivative (X; R = Ac, R′ = CO_2Me) which, although it could not be obtained crystalline, had the expected ultraviolet maximum at 250 mμ and no infrared band for a $>C{=}CH_2$ group. Ozonolysis gave the known [9] keto-acetate (XIII; R = Ac) as well as the same keto-ester (IX; R = Me) as was obtained in the earlier degradation.

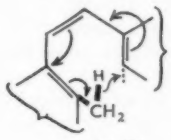


We were especially interested in the nature of the photochemically produced intermediate with ultraviolet absorption near 240 mμ. Although this is an abnormally short wavelength for a triene,[10] nevertheless we suspected that the compound had structure

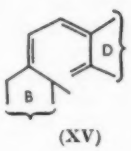
[8] Corey and Ursprung, *J. Amer. Chem. Soc.*, 1956, **78**, 183.
[9] Ruegg, Dreiding, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1950, **33**, 889.
[10] Inhoffen, Brückner, Gründel, and Quinkert, *Chem. Ber.*, 1954, **87**, 1407; Inhoffen and Quinkert, *ibid.*, p. 1418; Verloop, Koevoet, and Havinga, *Rec. Trav. chim.*, 1957, **76**, 689; Harrison and Lythgoe, *J.*, 1958, 837.

(V; R = Ac, R′ = CO_2Me). In the ursolic series neither the 240 mμ material nor its derivatives could be crystallised. Indeed, the compound is too easily isomerised thermally to permit extensive manipulation. In the α-amyrin series, on the other hand, the diene (IV; R = Ac, R′ = Me) furnishes on irradiation a similar maximum near 240 mμ which is unaffected in refluxing ethanol. By conversion into the 3,5-dinitrobenzoate a crystalline compound (V; R = acyl, R′ = Me) was obtained. This showed a nuclear magnetic resonance spectrum indicative of allylic methyl (2) and vinyl hydrogen (2) as in the assigned formula. Hydrolysis gave a non-crystalline alcohol (V; R = H, R′ = Me) with $\lambda_{max.}$ 240 mμ (ε 9200) and no infrared band for a $>C=CH_2$ group. This was selectively hydrogenated to a dihydro-derivative (VII; R = H, R′ = Me) which had no selective ultraviolet absorption and afforded a crystalline 3,5-dinitrobenzoate. The latter showed allylic methyl, but no vinyl hydrogen, in its nuclear magnetic resonance spectrum. Per-acid titration of the 3,5-dinitrobenzoate confirmed that two ethylenic linkages were present and that cyclopropane formation was not involved in the photo-isomerisation.

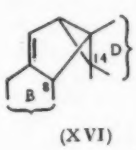
The photo-trienes (V; R = Ac, R′ = CO_2Me and Me) are assigned the expected *cis*-configuration, as already indicated, because irradiation with a tungsten lamp in the presence of iodine caused a shift of the maximum to longer wavelengths and greater intensities. This is a standard procedure for detecting a *cis*-isomer [11] and a suitable model experiment was run with calciferol to check our technique. The *cis*-configuration of the photo-trienes is so encumbered that the abnormal spectrum is readily understood. Indeed, the two methyl groups at positions 8 and 14 cannot be coplanar and it is possible that the 8-methyl group, which was originally β-oriented, retains its position above the 14-methyl group, which was originally α-oriented. This would explain the stereospecificity of the thermal rearrangement [see (XIV)] which would necessarily place hydrogen in the β-configuration at position 14 in the trienes, as in (VI). We cannot, however, explain why the other possible thermal isomerisation product (XV) is not formed in major amount, or why the photo-triene in the α-amyrin series (V; R = Ac, R′ = Me) is more stable than that in the ursolate series (V; R = Ac, R′ = CO_2Me).



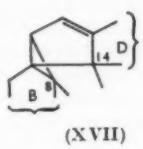
(XIV)



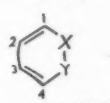
(XV)



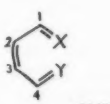
(XVI)



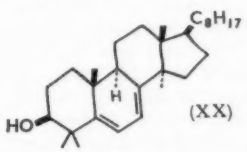
(XVII)



(XVIII)



(XIX)



(XX)

In summary, it may be said that the photochemistry of the triterpenoid homoannular ring c dienes parallels that of the steroidal dienes.[12] The analogy may well extend to the products described by Jeger, Redel, and Nowak.[5] We were able to show that over-irradiation of the triene (V; R = Ac, R′ = CO_2Me) gave the photo-isomer previously described. This well-crystallised product was not formed on over-irradiation of the triene (VI; R = Ac, R′ = CO_2Me). The absorption spectra of the over-irradiation products are comparable with those of the suprasterols.[13] If structural analogy also pertains then

[11] See, *inter al.*, Verloop, Koevoet, and Havinga, *Rec. Trav. chim.*, 1955, **74**, 1125; Inhoffen, Quinkert, Hess, and Erdmann, *Chem. Ber.*, 1956, **89**, 227; Verloop, Koevoet, van Moorselaar, and Havinga, *Rec. Trav. chim.*, 1959, **78**, 1004.

[12] See Havinga, de Koch, and Rappoldt, *Tetrahedron*, 1960, **11**, 276.

[13] Dauben, Bell, Hutton, Laws, Rheiner, and Urscheler, *J. Amer. Chem. Soc.*, 1958, **80**, 4116.

the compounds of Jeger, Redel, and Nowak [5] can be represented as in formula (XVI) or (XVII).

In our preliminary communication [1] we pointed out that the photochemical cleavage of steroidal ring B dienes, of triterpenoid ring C dienes, and of *ortho*-type cyclohexadienones [14] could all be fitted into a generalised scheme of the type (XVIII) ⟶ (XIX), a theme which we have developed further.[15] Obviously carbon atoms 1—4 can bear a wide variety of substituents and can themselves be replaced by other hetero-atoms. Also, there is considerable scope for variation in X and Y. Recently, it has been reported [16] that α-pyrones fall into this category, as does one example of a conjugated pyran.[17] So far as homoannular cyclohexadienes are concerned cyclohexa-1,3-diene behaves as expected,[18] as does α-phellandrene.[18] It will be of interest to see how far this simple structural theme can be developed.

The calciferol analogue (VI; R = H, R′ = CO_2Me) obtained by mild alkaline hydrolysis of the corresponding acetate had no significant biological activity (<1/10,000 that of calciferol). We report also that irradiation of 7-dehydro-4,4,14-trimethylcholesterol [19] (XX) gave a product with a similar lack of activity. We thank Messrs. Glaxo Laboratories Ltd. for these tests.

Experimental

M. p.s were taken on the Kofler block. Unless specified to the contrary, $[\alpha]_D$ refer to $CHCl_3$ and ultraviolet absorption spectra to EtOH solutions, and infrared absorption spectra to Nujol mulls. Microanalyses were carried out by Miss J. Cuckney and her colleagues. Light petroleum refers to the fraction of b. p. 40—60°. Nuclear magnetic resonance spectra were kindly determined and interpreted by Dr. J. W. Lown.

Irradiation of Methyl Dehydroursolate Acetate (IV; R = Ac, R = CO_2Me).—Methyl dehydroursolate acetate [20] (1·0 g.) in ethanol (400 ml.) was irradiated in a Pyrex-glass flask with a bare mercury-arc lamp (125 w). The flask was placed over the lamp so that the solvent refluxed gently. All irradiations were conducted under oxygen-free nitrogen. The course of the irradiation was determined by ultraviolet spectroscopy. The band at 283 mμ of the starting material declined and new bands appeared at ~240 and ~260 mμ. Irradiation was interrupted when the band at 260 mμ had ε ~10,000 and that at 240 mμ had ε ~8000. The 283 mμ band had by then essentially disappeared. The mixture was then refluxed under nitrogen for 2 hr., the 240 mμ band disappearing and the 260 mμ band attaining ε ~15,000. The combined ethanolic solutions from two such irradiations were concentrated *in vacuo* to about 25 ml. and left at room temperature for 12 hr. Starting material (about 250 mg.) crystallised and was removed. The filtrate, left at 0° overnight, gave prisms, m. p. 144—147°, $\lambda_{max.}$ 261 mμ (ε 18,000). Filtration and removal of the residual solvent *in vacuo* afforded a yellow gum which was chromatographed in light petroleum over acid-washed alumina (Grade II; 60 g.). Elution with 9 : 1 and 4 : 1 light petroleum–benzene gave oils with $\lambda_{max.}$ 240 mμ (ε 8200 and 7700 respectively) which were not examined further. Elution with 1 : 1 light petroleum–benzene gave further material, with $\lambda_{max.}$ at 261 mμ. This was combined with the product obtained by direct crystallisation (see above) (1·53 g.). Recrystallisation from ether–methanol gave *methyl pyrophotodehydroursolate acetate* (VI; R = Ac, R′ = CO_2Me) (57%), m. p. 152—153°, $[\alpha]_D$ −85° (*c* 0·87 in CCl_4), $\lambda_{max.}$ 215 and 261 mμ (ε 16,000 and 19,700 respectively), $\lambda_{min.}$ 230 mμ (ε 9400), $\nu_{max.}$ (in CCl_4) 1727, 1628, 1239, and 895 cm.$^{-1}$ (Found: C, 77·7; H, 9·85. $C_{33}H_{50}O_4$ requires C, 77·6; H, 9·85%).

Ozonolysis of Methyl Pyrophotodehydroursolate Acetate (VI; R = Ac, R′ = CO_2Me).—(a) *Characterisation of formaldehyde. The triene (53 mg.) in purified methylene dichloride (10 ml.*

[14] Barton and Quinkert, *Proc. Chem. Soc.*, 1958, 197; *J.*, 1960, 1.
[15] Barton, *Helv. Chim. Acta*, 1959, **42**, 2604.
[16] de Mayo, in "Advances in Organic Chemistry," ed. Raphael; Taylor, and Wynberg, Interscience Publ. Inc., New York, 1960, Vol. II, p. 394.
[17] Büchi and Yang, *Helv. Chim. Acta*, 1955, **38**, 1338; *J. Amer. Chem. Soc.*, 1957, **79**, 2318.
[18] de Koch, Minnaard, and Havinga, *Rec. Trav. chim.*, 1960, **79**, 922; see also Barton, ref. 15, and compare Srinivasan, *J. Amer. Chem. Soc.*, 1960, **82**, 5063.
[19] Barton and Thomas, *J.*, 1953, 1842.
[20] Ruzicka, Jeger, and Redel, *Helv. Chim. Acta*, 1943, **26**, 1235.

was ozonised at −60° for 30 min. Zinc dust (1·0 g.) was added with stirring and the mixture allowed to attain room temperature. After filtration into distilled water the product was steam-distilled into aqueous dimedone, and the methylene dichloride boiled off. This afforded the dimedone–formaldehyde derivative (6 mg.), identified by m. p., mixed m. p., and crystal form. A control experiment gave no formaldehyde.

(b) *Isolation of major fragments.* The triene (365 mg.) in dry ethyl acetate (70 ml.) was ozonised at −5° until all triene absorption had disappeared (2 hr.). Water (5 ml.) was added and the ethyl acetate boiled off. The aqueous solution was made alkaline with sodium carbonate and treated with 10% hydrogen peroxide (3 ml.) on the steam-bath for 10 min. Extraction with ether gave a neutral fraction (see below). Acidification and further extraction with ether gave an acidic fraction which crystallised from ethyl acetate–cyclohexane as prisms, m. p. 163—178° (68 mg.). Sublimation at 10^{-4} mm. and recrystallisation from ether–light petroleum afforded the *acetoxy-dicarboxylic acid* (VIII; R = Ac, R′ = H), m. p. 180—185°, $[\alpha]_D$ ±0° (*c* 1·07) (Found: C, 59·9; H, 8·15. $C_{15}H_{24}O_6$ requires C, 60·0; H, 8·05%). Saponification with 5% ethanolic potassium hydroxide under reflux gave the corresponding *hydroxy-dicarboxylic acid* (VIII; R = R′ = H), m. p. (rhombic prisms from ethyl acetate–chloroform) 214—217° decomp., $[\alpha]_D$ −9° (*c* 0·62 in dioxan) (Found: C, 60·45; H, 8·75. $C_{13}H_{22}O_5$ requires C, 60·45; H, 8·6%). Treatment with ethereal diazomethane and then with benzoyl chloride–pyridine afforded the corresponding *benzoate dimethyl ester* (VIII; R = Bz, R′ = Me). Recrystallised from methylene dichloride–light petroleum this formed needles, m. p. 100—101·5°, $[\alpha]_D$ +14° (*c* 2·40 in CCl_4), $\lambda_{max.}$ 230, 274, and 282 mμ (ε 12,700, 890, and 710 respectively) (Found: C, 67·85; H, 7·85. $C_{22}H_{30}O_6$ requires C, 67·65; H, 7·75%). Similarly methylation with ethereal diazomethane followed by 3,5-dinitrobenzoylation [21] gave the *dimethyl ester 3,5-dinitrobenzoate*. This crystallised from ether–light petroleum as needles, m. p. 100—102° (Found: C, 54·6; H, 5·6. $C_{22}H_{28}N_2O_{10}$ requires C, 55·0; H, 5·85%).

The neutral fraction from the ozonolysis (see above) was combined with that from a further ozonolysis of 242 mg. of triene to give a viscous, pale yellow oil (289 mg.). Distillation at 120°/4 × 10^{-5} mm. furnished the keto-ester (IX; R = Me) (125 mg.) as a colourless, viscous oil, $[\alpha]_D$ −27° (*c* 2·14), $\nu_{max.}$ (in CS_2) 1733 and 1710 cm.$^{-1}$. Saponification with an aqueous-ethanol (6 ml.; 80%) solution of potassium hydroxide (90 mg.) under reflux (oxygen-free nitrogen) for 3 hr. and separation into acidic and neutral fractions afforded, in the acidic portion, crystalline 1β,2α,7β-*trimethyl*-8-*oxo*-cis-*decalin*-4αβ-*carboxylic acid* (XII; R = H) (173 mg.). After sublimation at 120°/4 × 10^{-5} mm. and crystallisation from ether–light petroleum this formed irregular crystals which melted partially at 143° and then resolidified as plates, m. p. 160—163°, $[\alpha]_D$ −97° (*c* 2·24), $\nu_{max.}$ 1718 and 1681 cm.$^{-1}$ (Found: C, 70·75; H, 9·45. $C_{14}H_{22}O_3$ requires C, 70·55; H, 9·3%). Treatment with ethereal diazomethane gave the oily keto-ester (XII; R = Me), b. p. 118°/2 × 10^{-5} mm., $[\alpha]_D$ −108° (*c* 1·19).

Synthesis of Racemic Methyl β-(3β-*Benzoyloxy*-6α-*methoxycarbonyl*-2,4,6-*trimethyl*-β-*cyclohexyl*)*propionate* (VIII; R = Bz, R′ = Me).—The racemic ketone-benzoate [7] (XI; R = Bz) (21 mg.) was taken up in 0·0784N-chromium trioxide in acetic acid (8·4 ml.) and warmed on the steam-bath until an aliquot part showed that the theoretical amount of oxidant had been consumed. The excess of chromium trioxide was destroyed by sulphur dioxide, and the solvent removed *in vacuo*. Addition of water (1·0 ml.) and extraction into ether gave the dicarboxylic acid benzoate (VIII; R = Bz, R′ = H). Sublimation and crystallisation from ethyl acetate–cyclohexane furnished a specimen (44%), m. p. 198—200°, which with an excess of diazomethane gave the racemic *benzoate dimethyl ester* (VIII; R = Bz, R′ = Me). This formed needles (from methylene dichloride–light petroleum), m. p. 101—103°, mixed m. p. 95—103° with optically active material (Found: C, 67·7; H, 7·85. $C_{22}H_{30}O_6$ requires C, 67·65; H, 7·75%). The infrared spectra of the racemic and the optically active material were identical (CCl_4; 22 bands).

Methyl Dihydropyrophotodehydroursolate Acetate (X; R = Ac, R′ = CO_2Me).—Methyl pyrophotodehydroursolate acetate (VI; R = Ac, R′ = CO_2Me) (100 mg.) in ethanol (5 ml.) was hydrogenated over 10% palladised strontium carbonate (Johnson Matthey) until 1 mol. of hydrogen had been consumed. The product was chromatographed over alumina (Grade III; 5 g.). Elution with 1 : 10 ether–light petroleum and sublimation at 140°/2 × 10^{-5} mm. gave the required dihydro-compound (X; R = Ac, R′ = CO_2Me) as a colourless gum, $\lambda_{max.}$ 250 mμ (ε 12,800), $[\alpha]_D$ +82° (*c* 0·53), $\nu_{max.}$ 1724 and 1235 cm.$^{-1}$, no absorption at 893 cm.$^{-1}$.

This dihydro-compound (400 mg.) in methylene dichloride (25 ml.) was ozonised at −5°

[21] Brewster and Ciotti, *J. Amer. Chem. Soc.*, 1955, **77**, 6214.

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until the ultraviolet absorption band at 250 mμ had disappeared. Water (3 ml.) was added and the methylene dichloride removed *in vacuo*. The product was saponified with 1 : 5 aqueous-ethanolic potassium hydroxide (400 mg. in 24 ml.) under reflux (oxygen-free nitrogen) for 4 hr. and separated into acidic (160 mg.) and neutral (160 mg.) fractions. The acidic fraction, on sublimation and crystallisation from ether–light petroleum, gave the keto-acid (XII; R = H), identified by m. p., mixed m. p., crystal form, and infrared spectrum. The neutral fraction was acetylated with pyridine–acetic anhydride and then sublimed at 10^{-6} mm. to give crystalline acetoxy-ketone (XIII; R = Ac). Recrystallised from ether–light petroleum this formed needles, m. p. 128—129°, $[\alpha]_D$ −10° (*c* 0·70), $\nu_{max.}$ 1724 and 1703 cm.$^{-1}$ (Found: C, 72·45; H, 9·7. Calc. for $C_{16}H_{26}O_3$: C, 72·15; H, 9·85%). The constants given in the literature [9] are m. p. 128—129°, $[\alpha]_D$ −12° (*c* 0·76).

Photodehydro-α-amyrin 3,5-Dinitrobenzoate (V; R = 3,5-Dinitrobenzoyl, R′ = Me).—Dehydro-α-amyrin [20] (IV; R = H, R′ = Me) (500 mg.) was irradiated *in anhydrous ether* (400 ml.) as outlined above. The band at 281 mμ of the starting material declined and a new band appeared at 240 mμ reaching a maximum intensity of ε 8000—9000. Removal of solvent *in vacuo* gave a foam showing $\lambda_{max.}$ 240 mμ (ε 8200) with no infrared band near 890 cm.$^{-1}$. This material, which did not crystallise, was converted into its 3,5-dinitrobenzoate by Brewster and Ciotti's method.[21] Chromatography over alumina (Grade IV), elution with 1 : 1 light petroleum–benzene and crystallisation from methanol–acetone and then from acetone afforded *photodehydro-α-amyrin 3,5-dinitrobenzoate* (V; R = 3,5-dinitrobenzoyl, R′ = Me) as needles, m. p. 116—121°, $[\alpha]_D$ +335° (*c* 0·77 in CCl_4), $\lambda_{max.}$ 213 mμ (ε 51,200), shoulder at 220 mμ (ε 47,400), no infrared absorption at 890 cm.$^{-1}$ (Found: C, 71·7; H, 8·3. $C_{37}H_{50}N_2O_6$ requires C, 71·8; H, 8·15%).

Dihydrophotodehydro-α-amyrin 3,5-Dinitrobenzoate (VII; R = 3,5-Dinitrobenzoyl, R′ = Me).—Photodehydro-α-amyrin 3,5-dinitrobenzoate (see above) (72 mg.) was refluxed for 45 min. with aqueous-ethanolic 1% potassium hydroxide (5 ml.). The neutral product, photodehydro-α-amyrin, had $\lambda_{max.}$ 240 mμ (ε 9200) and no infrared band near 890 cm.$^{-1}$ but it did not crystallise. This product (98 mg.) in ethanol (5 ml.) was hydrogenated over 10% palladised charcoal (Baker) until 1·2 mol. had been taken up (good selectivity). The product, which had only end-absorption at 203 mμ (ε 10,000), was 3,5-dinitrobenzoylated as above. The product, chromatographed over alumina (Grade III) with elution by 1 : 1 light petroleum–benzene, crystallised from acetone–methanol, to give *dihydrophotodehydro-α-amyrin 3,5-dinitrobenzoate* (VII; R = 3,5-dinitrobenzoyl, R′ = Me) as needles, m. p. 163—164°, $\lambda_{max.}$ (in cyclohexane) 211 mμ (ε 33,580), shoulder 227 (ε 26,550) (Found: C, 71·4; H, 8·1; N, 4·3. $C_{37}H_{52}O_6N_2$ requires C, 71·6; H, 8·45; N, 4·5%). Titration with perphthalic acid showed the presence of two ethylenic linkages.

Iodine-catalysed Isomerisation of Photodehydro-α-amyrin.—Photodehydro-α-amyrin (V; R = H, R′ = Me) (4·8 mg.) in anhydrous ether (500 ml.) containing a trace of pyridine and iodine (0·01 mg.) was irradiated [11] with a tungsten lamp until maximum absorption was reached (45 min.). The irradiated solution, freed from iodine and pyridine, was evaporated to dryness *in vacuo* to an oil showing $\lambda_{max.}$ 253 mμ (ε 13,000).

In a parallel model experiment calciferol, $\lambda_{max.}$ 265 mμ (ε 18,000), was irradiated [11] as above. The product showed $\lambda_{max.}$ 272 mμ (ε 23,200).

Over-irradiation of Methyl Pyrophotodehydroursolate Acetate (VI; R = Ac, R′ = CO_2Me).—(*a*) Methyl dehydroursolate acetate (IV; R = Ac, R′ = Me) (244 mg.) in anhydrous ether (300 ml.) was irradiated in a Pyrex flask (500 ml.) cooled under running water so that the temperature of the solution did not exceed 10°. During the irradiation the ultraviolet absorption maximum changed from 282 mμ to that expected of methyl photodehydroursolate acetate (V; R = Ac, R′ = Me) [$\lambda_{max.}$ 240 mμ (ε 10,000), $\lambda_{min.}$ 230 mμ (ε 9900) end-absorption] and then, on continued irradiation, the absorption at 240 mμ declined and the spectrum changed to that of methyl lumidehydroursolate acetate (see below). The ether was removed *in vacuo* and the product crystallised from acetone–methanol, to furnish methyl lumidehydroursolate acetate (52 mg.), m. p. 163—164°, end absorption with ε 9300 at 220 mμ and 1100 at 250 mμ. In a second experiment in which the ether was allowed to reflux during the irradiation methyl dehydroursolate acetate (102 mg.) gave the same methyl lumidehydroursolate acetate (44 mg.) (Found: C, 77·85; H, 9·4. Calc. for $C_{33}H_{50}O_4$: C, 77·6; H, 9·85%). Jeger, Redel, and Nowak [5] record m. p. 162—163° for the latter compound.

(*b*) Methyl pyrophotodehydroursolate acetate (VI; R = Ac, R′ = Me) (244 mg.) was irradiated <10° as described above. The absorption of the triene changed smoothly to a

broad curve showing end-absorption only, with ε 8600 at 220 mμ. Removal of the solvent *in vacuo* gave an oil which did not crystallise even after chromatography. The various fractions showed infrared spectra lacking several bands characteristic of methyl lumidehydroursolate acetate.

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IMPERIAL COLLEGE, LONDON, S.W.7. [*Received, February 13th,* 1961.]

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649. *The Synthesis of 3-Oxototaryl Methyl Ether.*

By D. A. H. TAYLOR.

(±)-3-Oxototaryl methyl ether (IXb) has been synthesised from 2-naphthol by way of 5-isopropyl-6-methoxy-1-tetralone. This was converted by standard methods into 1,2,3,4,9,12-hexahydro-8-isopropyl-7-methoxy-1,1,12-trimethyl-2-oxophenanthrene (VIII), which on hydrogenation over palladised charcoal gave a mixture that on reoxidation and chromatography yielded (±)-3-oxototaryl methyl ether, identical in infrared spectrum with material of natural origin.

A DITERPENE isolated by Chow and Erdtmann [1] from the wood of *Tetraclinis articulata* has been shown to be 3-oxototarol (IXa). The present author was informed of this before publication, and enabled to carry out a synthesis.

The scheme shown below, based on the recent general hexahydro-oxophenanthrene synthesis by Howell and Taylor,[2] was devised and has now been completed.

1-Bromo-2-methoxynaphthalene (I) was converted into the Grignard reagent, best in tetrahydrofuran, and this with acetone gave a mixture of 1-isopropenyl-2-methoxynaphthalene (II) and 2-methoxynaphthalene. These could not be separated, but after hydrogenation over Adams catalyst fractionation readily gave crystalline 1-isopropyl-2-methoxynaphthalene. The hydrogenation was slow, and it was found better to continue the synthesis with the mixture. This was hydrogenated over Raney nickel at 120° to give 1,2,3,4-tetrahydro-5-isopropyl-6-methoxynaphthalene (III), which on oxidation with chromic acid in acetic acid below 20° gave 5-isopropyl-6-methoxy-1-tetralone (IV), obtained crystalline after fractionation. When this was treated with methylmagnesium bromide in ether the intermediate tertiary alcohol was dehydrated in the course of the reaction, and the product was 3,4-dihydro-5-isopropyl-6-methoxy-1-methylnaphthalene (V). Perbenzoic acid oxidised this to the 2-tetralone (VI), which with 4-chlorobutan-2-one afforded the hexahydrophenanthrene (VIIa). The corresponding 4-methyl derivative (VIIb) was obtained by the use of 1-chloropentan-3-one, but the yield was lower.

Each of these compounds (VII) was readily methylated with methyl iodide and potassium t-butoxide [3] to give the *gem*-dimethyl derivative (VIII). Hydrogenation over neutral Adams catalyst then reduced only the carbonyl group, giving the alcohol (XII), identical with a sample obtained by reduction with sodium borohydride and reoxidised to the ketone (VIII) by chromic acid in acetone.[4] Hydrogenation of the ketone (VIII) over palladised charcoal in dilute methanolic acetic acid gave a complex mixture, which

[1] Chow and Erdtmann, *Acta Chem. Scand.*, 1960, **14**, 1852.
[2] Howell and Taylor, *J.*, 1958, 1248.
[3] Woodward, Patchett, Barton, Ives, and Kelly, *J.*, 1957, 1131.
[4] Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2548.

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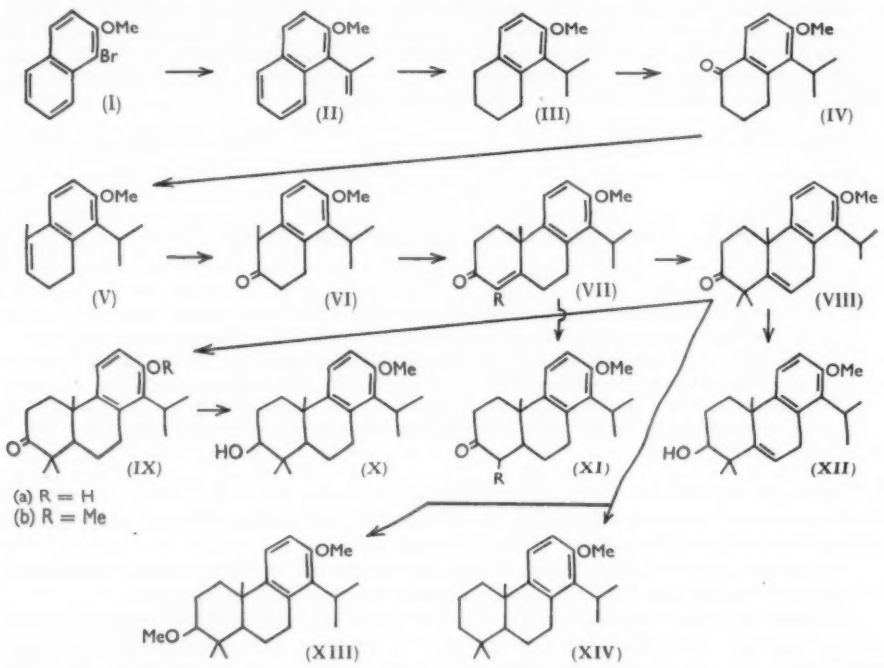
after reoxidation with chromic acid in acetone was chromatographed. Elution with hexane–benzene gave three crystalline components, and partly crystalline intermediate fractions suggested the presence of at least two more. The first substance isolated was (±)-totaryl methyl ether (XIV), m. p. 95—98°, identical in infrared spectrum with a sample prepared by methylating natural totarol.[5] The production of totarol methyl



ether in this way is paralleled in the reduction of cholesterol,[6] which gives a small yield of cholestane. Presumably in both cases the reduction proceeds through a homoallylic bridged ion, similar to that postulated by Winstein's school[7] to explain the kinetics of the solvolysis of cholesteryl toluene-*p*-sulphonate. The second substance crystallised from methanol in plates, m. p. 136°, and gave analytical figures corresponding to a dimethyl ether (XIII). If this arises through the bridged ion, as seems probable, then it may also be the product of a homoallylic rearrangement, and have the methoxyl group in the 6-position. The third substance isolated crystalline was (±)-3-oxototaryl methyl ether, m. p. 102—103°, identical in infrared spectrum with a sample prepared by Dr. Chow from natural 3-oxototarol.

Experimental

1-Isopropyl-2-methoxynaphthalene.—1-Bromo-2-methoxynaphthalene (238 g.) in benzene (1 l.) was added to magnesium (40 g.) in ether (2 l.). The thick suspension was stirred and acetone (50 ml.) added dropwise, after which there was no further reaction. The mixture was treated with dilute hydrochloric acid, and the organic layer was separated and distilled. The product was collected as an oil at 136°/4 mm.; it contained no bromine. It was dissolved

[5] Short and Stromberg, *J.*, 1937, 516.
[6] Hershberg, Oliveto, Rubin, Stäudle, and Kuhlen, *J. Amer. Chem. Soc.*, 1951, **73**, 1144.
[7] Winstein and Adams, *J. Amer. Chem. Soc.*, 1948, **70**, 838; Simonetta and Winstein, *J. Amer. Chem. Soc.*, 1954, **76**, 18.

in methanol and hydrogenated over Adams catalyst; after filtration the solvent was evaporated and the residue fractionated. 2-Methoxynaphthalene, m. p. and mixed m. p. 72°, was collected at 130°/4 mm., followed by *1-isopropyl-2-methoxynaphthalene* (65 g.) at 144°/4 mm. Crystallisation from methanol gave the analytical sample, m. p. 48—49° (Found: C, 83·3; H, 8·1. $C_{14}H_{16}O$ requires C, 84·0; H, 8·05%).

5-Isopropyl-6-methoxy-1-tetralone (IV).—1-Bromo-2-methoxynaphthalene (700 g.) dissolved in tetrahydrofuran (2 l.) was added dropwise to magnesium (120 g.) in tetrahydrofuran (1 l.). Then the clear solution was stirred while acetone (250 ml.) was added. The complex was decomposed with aqueous hydrochloric acid, the organic layer separated and washed with water, the solvent evaporated, and the residue distilled in a vacuum. The product (580 g.) was obtained as an oil, b. p. 130—140°/4 mm. This was hydrogenated over Raney nickel catalyst at 120°/100 atm. (initial) until hydrogen uptake was complete. After filtration and redistillation, the crude product was dissolved in acetic acid (2 l.), and a solution of chromic acid (420 g.) in water (150 ml.) and acetic acid (1 l.) was added at such a rate that the temperature was held at ~ 15°. The mixture was allowed to warm to room temperature (30°) overnight and then diluted with water and ether. The organic layer was washed and evaporated, and the residue distilled (the tail fraction partly crystallised) and then fractionated. *5-Isopropyl-6-methoxy-1-tetralone* was collected at 160—170°/2 mm. as an oil which mostly crystallised. Recrystallisation from pentane, followed by refractionation of the residues, gave the pure ketone (183 g., 28%) as pale yellow prisms, m. p. 74° (Found: C, 76·9; H, 8·2. $C_{14}H_{18}O_2$ requires C, 77·0; H, 8·3%).

3,4-Dihydro-5-isopropyl-6-methoxy-1-methylnaphthalene (V).—To a Grignard solution, prepared in ether from magnesium (24 g.) and an excess of methyl bromide, was added the above ketone (107 g.) in ether. After being worked up in the usual way, the product was distilled at 140°/2 mm., and then crystallised from methanol–ether. *3,4-Dihydro-5-isopropyl-6-methoxy-1-methylnaphthalene* (89 g., 84%) formed colourless plates, m. p. 60—61° (Found: C, 83·15; H, 9·1. $C_{15}H_{20}O$ requires C, 83·3; H, 9·3%), $\lambda_{max.}$ (in MeOH) 268 mμ (log ε 3·9).

5-Isopropyl-6-methoxy-1-methyl-2-tetralone (VI).—The above dihydronaphthalene (63 g.), dissolved in chloroform (100 ml.), was oxidised with perbenzoic acid (39 g.) in chloroform (550 ml.) at <10°. After storage overnight in the refrigerator, the red solution was washed with sodium hydroxide solution and with water and evaporated. The residue was refluxed for 1·5 hr. with sulphuric acid (60 ml.), methanol (400 ml.), and water (320 ml.), and the product isolated with ether and distilled. 5-Isopropyl-6-methoxy-1-methyl-2-tetralone (55 g., 80%) was collected at 164°/2 mm. as a colourless oil. The *semicarbazone* formed crystals, m. p. 190°, from ethanol (Found: C, 66·5; H, 8·4. $C_{16}H_{23}N_3O_2$ requires C, 66·4; H, 8·0%).

2,3,4,9,10,12-Hexahydro-8-isopropyl-7-methoxy-12-methyl-2-oxophenanthrene (VIIa).—Sodium hydride (10 g. of a 50% suspension in oil) was stirred with cyclohexane (200 ml.) under nitrogen, and the above ketone (50 g.) in cyclohexane (100 ml.) added slowly. After 10 minutes' stirring 4-chlorobutan-2-one (20 g.) was added dropwise. After the vigorous reaction was over, another portion of sodium hydride (10 g. of 50%) was added cautiously, and the whole stirred and refluxed for 15 min. Methanol (20 ml.) was then added, and, after 5 min., dilute hydrochloric acid. The organic layer was dried and run through a column of alumina (900 g.). After being washed with light petroleum to remove the oil introduced with the sodium hydride, the column was eluted with ether. Evaporation of the ether left a residue which from hexane gave *2,3,4,9,10,12-hexahydro-8-isopropyl-7-methoxy-12-methyl-2-oxophenanthrene* (22 g., 36%) as off-white prisms, m. p. 105—106° (Found: C, 80·2; H, 8·0. $C_{19}H_{24}O_2$ requires C, 80·2; H, 8·5%), $\lambda_{max.}$ (in MeOH) 235 mμ (log ε 4·5), $\nu_{max.}$ (in Nujol) 1667 cm.$^{-1}$.

2,3,4,9,10,12-Hexahydro-8-isopropyl-7-methoxy-1,12-dimethyl-2-oxophenanthrene (VIIb).—A similar preparation with the 2-tetralone (27 g.) and 1-chloropentan-3-one (12·5 g.) gave *2,3,4,9,10,12-hexahydro-8-isopropyl-7-methoxy-1,12-dimethyl-2-oxophenanthrene* (9·8 g.), crystallising from methanol in colourless prisms, double m. p. 85—86°/108—109° (Found: C, 81·0; H, 8·9. $C_{20}H_{26}O_2$ requires C, 80·5; H, 8·8%), $\lambda_{max.}$ (in MeOH) 232 (log ε 4·04), 245 mμ (log ε 4·07), $\nu_{max.}$ (in Nujol) 1667 cm.$^{-1}$.

1,2,3,4,9,10,11,12-Octahydro-8-isopropyl-7-methoxy-12-methyl-2-oxophenanthrene (XIa).—The hexahydro-compound (VIIa) (6·5 g.) in ether (100 ml.) was added to a solution of sodium (2 g.) in liquid ammonia (200 ml.). After 5 min. ammonium chloride was added, then ether and water. The ether layer was washed and evaporated; the residue crystallised from methanol to give *1,2,3,4,9,10,11,12-octahydro-8-isopropyl-7-methoxy-12-methyl-2-oxophenanthrene* (4·3 g.)

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as colourless plates, m. p. 112—113° (Found: C, 79·5; H, 9·1. $C_{19}H_{26}O_2$ requires C, 79·7; H, 9·1%), $\nu_{max.}$ (in Nujol) 1705 cm.$^{-1}$.

1,2,3,4,9,10,11,12-Octahydro-8-isopropyl-7-methoxy-1,12-dimethyl-2-oxophenanthrene (XIb).—Reduction of the hexahydro-compound (VIIb) (8·3 g.) as above gave the *octahydro-ketone* (XIb) (5·5 g.), prisms (from methanol), m. p. 116° (Found: C, 80·2; H, 9·2. $C_{20}H_{28}O_2$ requires C, 80·0; H, 9·4%), $\nu_{max.}$ (in Nujol) 1705 cm.$^{-1}$.

1,2,3,4,9,12-Hexahydro-8-isopropyl-7-methoxy-1,1,12-trimethyl-2-oxophenanthrene (VIII).—Potassium (1 g.) was dissolved in t-butyl alcohol (70 ml.), and 2,3,4,9,10,12-hexahydro-8-isopropyl-7-methoxy-12-methyl-2-oxophenanthrene (VIIa) (3 g.) was added. After a few minutes methyl iodide (5 ml.) was added and the solution refluxed for 30 min. After evaporation in a vacuum the residue was taken up in water and ether, and the ether layer evaporated. Crystallisation from methanol gave the *1,1,12-trimethyl derivative* (1·9 g., 60%) as colourless prisms, m. p. 112° (Found: C, 80·7; H, 9·2. $C_{21}H_{28}O_2$ requires C, 80·7; H, 9·0%), $\nu_{max.}$ (in Nujol) 1705 cm.$^{-1}$.

1,2,3,4,9,12-Hexahydro-2-hydroxy-8-isopropyl-7-methoxy-1,1,12-trimethylphenanthrene (XII).—The ketone (VIII) (700 mg.) in methanol (10 ml.) was treated with sodium borohydride (52 mg.) in a little water. After 1 hr. more borohydride (25 mg.) was added, and after a further hour the solution was diluted with aqueous sulphuric acid. The precipitate was collected and crystallised from hexane to give *1,2,3,4,9,12-hexahydro-2-hydroxy-8-isopropyl-7-methoxy-1,1,12-trimethylphenanthrene* (630 mg.) as needles, m. p. 119—120° (Found: C, 80·3; H, 9·8. $C_{21}H_{30}O_2$ requires C, 80·2; H, 9·6%).

(±)-*3-Oxototaryl Methyl Ether* (IX).—The unsaturated trimethyl ketone (VIII) (1·0 g.) was hydrogenated in methanol (50 ml.) and acetic acid (1 ml.) over palladised charcoal (500 mg.). Hydrogen uptake was rapid, and ceased after the absorption of 140 ml. The solution was then filtered from catalyst and evaporated, the residue was dissolved in ether, filtered from a little insoluble material, washed until neutral, and recovered. The residue was dissolved in acetone (25 ml.) and oxidised with 8N-chromic acid (about 1 ml.) until an orange colour persisted. The solution was then diluted with water and ether, the organic layer evaporated, and the product chromatographed on alumina (30 g. of type H). Elution with hexane and then with hexane–benzene gave the following three substances in order of elution from the column: (a) (±)-*totaryl methyl ether* (XIV) (25·6 mg.), plates, m. p. 95—98°, from ether–methanol (Found: 83·7; H, 11·0. $C_{21}H_{32}O$ requires: C, 83·9; H, 10·7%). The infrared spectrum was identical with that of a specimen of natural totaryl methyl ether; (b) (±)-3(?)-*methoxytotaryl methyl ether* (XIII) (162 mg.), plates (from methanol), m. p. 136° (Found: C, 79·95; H, 10·5. $C_{22}H_{34}O_2$ requires: C, 79·95; H, 10·4%); (c) (±)-*3-oxototaryl methyl ether* (IX) (173 mg.), prisms, m. p. 102—103° (from methanol) (Found: C, 80·3; H, 10·0. $C_{21}H_{30}O_2$ requires C, 80·2; H, 9·6%). The infrared spectrum of fraction (c) was identical with that of natural 3-oxototaryl methyl ether. The oily mother-liquors from the chromatography were combined and reduced with sodium borohydride. Chromatography of the product gave (±)-*totaradiol methyl ether* (X) (140 mg.), needles, m. p. 160° (from methanol) (Found: C, 79·3; H, 10·3. $C_{21}H_{32}O_2$ requires C, 79·7; H, 10·2%). This was identical with a sample produced by the reduction of pure (±)-3-oxototaryl methyl ether, and 3-oxototaryl methyl ether was recovered after oxidation with chromic acid in acetone.

The author is grateful to Dr. Yuan-Lang Chow for information, for specimens of natural products, and for comparing the infrared spectra of natural and synthetic oxototaryl methyl ether. Microanalyses are by Patrick Mowete of this department.

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650. *The Halides of the Transition Elements of the First Long Period.*

By M. Barber, J. W. Linnett, and N. H. Taylor.

The simple formula developed by Kapustinskii is used to calculate the lattice energies, and hence the heats of formation of the solid mono-, di-, and tri-halides of the elements from scandium to zinc in the Periodic Table. From these results the relative stabilities to be expected for the different valency states are determined and compared with experiment. It is found that the expected behaviour agrees well with observation, confirming the usefulness of Kapustinskii's formula.

Kapustinskii [1] has given formulæ for calculating the lattice energies of ionic crystals. In this paper, one of these is applied to the mono-, di-, and tri-halides of the elements from scandium to zinc. Some of these compounds are known and some are not, whilst others, *e.g.*, CuF, have been reported in the literature, only to have doubts thrown upon their method of preparation, etc. The existence, non-existence, and stability of the various halides are discussed in the light of the calculated results.

The lattice energies obtained are combined with other data to calculate, in particular, the heats of the following reactions:

$$MX \longrightarrow M + \tfrac{1}{2}X_2 + \Delta H_{1a} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1a)$$

$$MX \longrightarrow \tfrac{1}{2}MX_2 + \tfrac{1}{2}M + \Delta H_{1b} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1b)$$

$$MX_2 \longrightarrow MX + \tfrac{1}{2}X_2 + \Delta H_{2a} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2a)$$

$$MX_2 \longrightarrow \tfrac{2}{3}MX_3 + \tfrac{1}{3}M + \Delta H_{2b} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2b)$$

$$MX_3 \longrightarrow MX_2 + \tfrac{1}{2}X_2 + \Delta H_{3a} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3a)$$

where M and X represent the metal and halogen atoms, respectively.

It is also possible to calculate the heats involved in the reactions:

$$M + HX \longrightarrow MX + \tfrac{1}{2}H_2 + \Delta H_{1c} \quad . \quad . \quad . \quad . \quad . \quad . \quad (1c)$$

$$MX + HX \longrightarrow MX_2 + \tfrac{1}{2}H_2 + \Delta H_{2c} \quad . \quad . \quad . \quad . \quad . \quad . \quad (2c)$$

$$MX_2 + HX \longrightarrow MX_3 + \tfrac{1}{2}H_2 + \Delta H_{3c} \quad . \quad . \quad . \quad . \quad . \quad . \quad (3c)$$

If $$\tfrac{1}{2}H_2 + \tfrac{1}{2}X_2 \longrightarrow HX + \Delta H'$$

then $$\Delta H_{1a} + \Delta H' + \Delta H_{1c} = 0$$

$$\Delta H_{2a} + \Delta H' + \Delta H_{2c} = 0$$

$$\Delta H_{3a} + \Delta H' + \Delta H_{3c} = 0$$

For X = F, Cl, Br, and I, $\Delta H' = -64$, -22, -12, and -1 kcal./mole.[2]

Reactions (2a) and (2b) relate to the conversion of MX_2 into the lower halide MX and the higher halide MX_3. The heats of these processes will be important factors in the stability of MX_2. Reactions (1a) and (1b) are the analogous pair of reactions for MX, while reaction (3a) represents the decomposition of MX_3. The heats involved in (1c), (2c), and (3c) are important in deciding which halide will be formed by the action of the hydrogen halide on the metal.

Calculations and Results

The formula used for calculating the lattice energies U_n was Kapustinskii's simplest one:

$$U_n = 256{\cdot}1 \sum nZ_+Z_-/(r_+ + r_-)$$

[1] Kapustinskii, *Quart. Rev.*, 1956, **10**, 283.
[2] Cottrell, "The Strengths of Chemical Bonds," Butterworths, London, 1958.

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where Z_+ and Z_- are the ionic charges, n is the number of ions in the " molecule," and r_+ and r_- are the ionic radii of the species involved, referred to a co-ordination number of 6. The empirical basis of this expression is discussed by Kapustinskii.[1] Values used for the ionic radii are listed in Table 1. For certain of the metal ions, some of which are unknown, *e.g.* Sc^{++}, calculations were made for the two extreme values of the radii; the extremes are shown in Table 1, where it will be seen that widely spaced limits were used. The ionisation potentials and latent heats of the metals examined are listed in Table 2. In addition to the above data the quantity $(E - \frac{1}{2}D)$ is required for each halogen, where E is the electron affinity, and D is the dissociation energy of the diatomic molecule. For F, Cl, Br, and I, $(E - \frac{1}{2}D)$ was taken to be 66·3, 63·6, 60·2, and 53·8 kcal./mole, respectively. It is worth noting that the range of this quantity for the different halogens is small.

The heats of formation of the different halides can now be calculated by using a Born–Haber cycle. This gives the general formula

$$U_n - \sum I_n + n(E - \tfrac{1}{2}D) - L + \Delta H_n = 0$$

where U_n is the lattice energy associated with the halide of the metal in the nth valency state; $\sum I_n$ is the sum of the first n ionisation potentials; E and D have the same meaning as above; L is the latent heat of vaporisation of the metal at room temperature; and ΔH_n is the heat of formation of the nth halide, so that

$$\Delta H_n = \sum I_n + L - n(E - \tfrac{1}{2}D) - U_n$$

These heats are listed in Table 3; the values in parentheses are those obtained for the extreme values of the ionic radii used. The heats of the reactions listed in the introduction can then be derived by the application of Hess's law to the data given in Table 3, the results being presented graphically in Figs. 1—12. There are three figures for each halogen, one relating to the stability of MX, one to MX_2, and one to MX_3. The heats of reactions

TABLE 1. *Ionic radii of the metal ions. For* F^-, Cr^-, Br^-, *and* I^-, 1·36, 1·81, 1·95, *and* 2·16 Å *were used.**

	M^+	M^{2+}	M^{3+}
Sc	1·06	0·82—1·00	0·81
Ti	0·96	0·70—0·93	0·69
V	0·88	0·68—0·86	0·66
Cr	0·81	0·66—0·80	0·64
Mn	0·75—0·81	0·80	0·62
Fe	0·75—0·80	0·75	0·60
Co	0·75—0·85	0·72	0·57—0·60
Ni	0·75—0·90	0·70	0·54—0·60
Cu	0·96	0·72—0·80	0·60—0·70
Zn	0·88	0·74	0·60—0·70

* Pauling, " Nature of the Chemical Bond," Cornell Univ. Press, 1948.

TABLE 2. *The latent heats* (L) *and first, second, and third ionisation potentials* (I) *of the metals in kcal./g.-atom.**

	L	I_1	I_2	I_3		L	I_1	I_2	I_3
Sc	93	151	298	570	Fe	99	182	373	707
Ti	112	158	314	649	Co	102	181	393	773
V	122	155	328	685	Ni	101	176	419	833
Cr	94	156	380	714	Cu	81	178	468	849
Mn	68	171	361	777	Zn	31	217	414	915

* U.S. Bureau of Standards, Circulars 467, T. L. Cottrell, " Strengths of Chemical Bonds," Butterworths, 1958, for ionization potentials and latent heats, respectively.

(1c), (2c), and (3c), can be obtained arithmetically from these figures by making use of the values of $\Delta H'$ given in the Introduction. The data presented in Figs. 1 to 12, which constitute the main results of our calculations, will now be discussed.

Calculations of this type have been carried out by Grimm and Herzfeld [3] to demonstrate why salts such as sodium difluoride do not exist, but calculations were not made for the halides of the transition metals.

TABLE 3. *The calculated heats of formation of the halides (kcal./mole).*

	MF	MF_2	MF_3	MCl	MCl_2	MCl_3	MBr	MBr_2	MBr_3	MI	MI_2	MI_3
Sc	−34	−244 −297	−503	+2	−133 −170	−252	+14	−100 −134	−181	+31	−52 −81	−84
Ti	−28	−220 −295	−465	+20	−104 −155	−187	+33	−70 −116	−111	+52	−21 −61	−6
V	−18	−220 −281	−431	+23	−88 −135	−145	+36	−62 −99	−67	+54	−12 −44	+39
Cr	−52	−214 −264	−392	−9	−86 −119	−101	+4	−49 −79	−22	+24	+3 −23	+85
Mn	−63 −70	−244	−375	−20 −25	−116	−79	−7 −11	−79	+1	+13 +9	−27	+110
Fe	−22 −28	−208	−407	+21 +17	−73	−105	+35 +31	−35	−25	+54 +51	+18	+86
Co	−15 −26	−195	−320 −343	+26 +19	−59	−18 −34	+44 +33	−20	+62 +49	+59 +53	+34	+174 +162
Ni	−16 −32	−84	−239 −288	+24 +13	−44	+63 +30	+37 +27	−5	+143 +115	+55 +47	+51	+254 +231
Cu	−28	−117 −144	−115 −192	+10	+11 −8	+161 +110	+23	+48 +31	+236 +190	+41	+100 +85	+341 +301
Zn	−48	−203	−114 −191	−7	−68	+162 +111	+6	−29	+237 +191	+25	+24	+342 +302

DISCUSSION

The present calculations refer only to heats of reaction at room temperature. Thermodynamic stability is also dependent on entropy change, while the possibility of isolating and preserving a material is dependent on the energy of activation of processes that might lead to its changing to other compounds. As regards the former, the entropy factor is likely to be negligible for reactions (1b) and (2b) since only condensed substances are involved [1] but for reactions (1a), (2a), and (3a), the decomposition reactions will be favoured by the entropy factor, since *gaseous* halogens are evolved. These limitations to what has been done must be borne in mind when considering the deductions made from our results.

Before detailed consideration of how successful the present method is for understanding the stability of the various halides, the calculated heats of formation listed in Table 3 will be compared with experimental values.[4] It is found that the heats of formation of the dichlorides of the elements from titanium to cobalt are calculated satisfactorily: *e.g.* (observed results first, calculated figures in parentheses), $TiCl_2$ −121 (−104 to −155); VCl_2 −108 (−88 to −135); $CrCl_2$ −95 (−86 to −119); $MnCl_2$ −115 (−116); $FeCl_2$ −82 (−73); $CoCl_2$ −78 (−59). These results must be regarded as surprisingly good, bearing in mind that they are obtained as the difference between two large quantities, namely the energy expended on producing the ions, which is of the order of 600 kcal./mole, and the calculated lattice energy which is rather bigger than this. For $NiCl_2$ the comparison is: −76 (−44); for $CuCl_2$ −49 (−8 to +11); for $ZnCl_2$ −99 (−68). These discrepancies are about 30 kcal. for $NiCl_2$ and $ZnCl_2$ and about 50 for $CuCl_2$. They probably arise because more covalent bonding is involved in these than in the earlier dichlorides; it is known that in cupric chloride, where the discrepancy is the greatest, the binding is considerably covalent. This leads to an added stability. For the trichlorides the corresponding figures are: $ScCl_3$ −221 (−252); $TiCl_3$ −171 (−187); VCl_3 −137 (−145); $CrCl_3$ −135 (−101); $FeCl_3$ −97 (−105). Considering that these are obtained as the difference between two numbers both of which are greater than 1000 kcal., the agreement must be regarded as excellent.

[3] Grimm and Herzfeld, *Z. Physik*, 1923, **19**, 141.

[4] U.S. Bureau of Standards, Circular 500, 1952, except that the data for the titanium chlorides were taken from Altman, Farber, and Mason, *J. Chem. Phys.*, 1956, **25**, 531, and those for the chromium iodides from Gregory and Burton, *J. Amer. Chem. Soc.*, 1953, **75**, 6054.

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For the heats of formation of the dibromides (from solid metal and gaseous bromine) the following comparison can be made: $TiBr_2$ −102 (−70 to −116); $MnBr_2$ −98 (−79); $FeBr_2$ −67 (−35); $CoBr_2$ −62 (−20); $NiBr_2$ −61 (−5); $CuBr_2$ −40 (+31 to +48); $ZnBr_2$ −85 (−29). It will be seen that the discrepancies are greater than for the dichlorides, the dibromides being in fact more stable relative to the elements than is calculated. This is presumably because there is more covalent binding in the bromides than in the chlorides and again the discrepancy is greatest for the copper salt, which is to be expected. For the two tribromides the figures are: $ScBr_3$ −190 (−181); $TiBr_3$ −143 (−111). The agreement is surprisingly good (cf. $TiBr_2$). In agreement with the conclusion that the differences between calculated and observed heats of formation result from covalent character, it is found that the discrepancies are even greater for the di-iodides (from gaseous iodine also): TiI_2 −76 (−21 to −61); CrI_2 −52 (+3 to −23); MnI_2 −74 (−27); FeI_2 −45 (+18); CoI_2 −39 (+34); NiI_2 −36 (+51); CuI_2 −17 (+85 to +100); ZnI_2 −65 (+24). It does seem, therefore, that the later members of this di-iodide series are only stable to decomposition to the elements because of the covalent character of the binding in the crystals. For the tri-iodides only three heats of formation are known, and the comparison for these are: TiI_3 −103 (−6); CrI_3 −50 (+39). In both cases the discrepancy is large (about 90 kcal.), the tri-iodides being much more stable than calculated. This is presumably due again to the very high degree of covalent character arising from the high charge on the cation and large size of the anion. However, in calculating the stability relative to the di-iodides, differences are involved and consequently the discrepancy between theory and observation may be less than would be expected from the above figures. The differences between theory and experiment for the difluorides are in the reverse sense from those for the di-iodides, and this must be because there is less covalent binding in the fluorides than in the chlorides. The figures are: TiF_2 −198 (−220 to −295); CrF_2 −181 (−214 to −264); MnF_2 −189 (−244); CoF_2 −159 (−195); NiF_2 −159 (−184); CuF_2 −127 (−117 to −144); ZnF_2 −188 (−203). For the trifluorides the discrepancies are very much larger though it must be realised that for these the calculated lattice energies are of the order of 1500—2000 kcal. The three comparisons that can be made are: TiF_3 −315 (−465); CrF_3 −265 (−292); CoF_3 −187 (−320 to −343). It is clear therefore that the present calculations will give an exaggerated impression of the stability of the trifluorides.

Finally, the figures for the monohalides of copper are: CuCl −32 (+10); CuBr −29 (+23); CuI −23 (+41). The differences are 42, 52, and 64. The sequence is regular and the numbers suggest that some covalent bonding is involved. The corresponding discrepancies for the dihalides are greater. These results can be explained if the extent of covalency increases with the charge on the cation and the polarisability of the anion. These results are a natural consequence of the effects summarised in Fajans's rules. From the above it seems that the constant in Kapustinskii's empirical formula is such that the heats of formation of the chlorides are calculated quite accurately. The bromides and particularly the iodides tend to be more exothermic than the formula would suggest, while the fluorides tend to be less exothermic. Kapustinskii's formula, therefore, appears to be adjusted to allow for a certain amount of covalent bonding. However, in the results that follow, we shall be concerned more with the heats of interconversion of the halides of the different valency states so there will be some cancelling of the errors. These considerations suggest that it would be expected that the predictions for the chlorides are likely to be good. For the bromides the figures are likely to underestimate the stability of the halides and to favour slightly the lower halides, relative to the higher ones, more than is found in practice. The situation for the iodides will be similar but the effects are likely to be somewhat greater. For the fluorides the reverse will tend to be true, the stability of the higher fluorides (the trifluorides) being somewhat exaggerated. We shall see that these conclusions are, in fact, borne out though the correspondence between prediction and fact is, broadly speaking, astoundingly good.

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It is interesting to compare the results obtained here with those of the detailed calculations by Waddington [5] on copper monofluoride. By using Pauling's value for the ionic radius, and assuming first a sodium chloride structure, he calculated the lattice energy to be 209 kcal./mole, whilst on a zinc blende model it becomes equal to 232 kcal./mole. Our value is 221 kcal./mole. Waddington also derives a value for the heat of formation of copper monofluoride and finds it in the first case (sodium chloride structure) to be −14 kcal./mole, and in the second case −36 kcal./mole. Our lattice energy gives it a value of −28 kcal./mole. The results, as can be seen, are in quite good agreement, allowance being made for the value of $(E - \frac{1}{2}D)$ for the fluorine molecule which he uses, namely 64·8 as opposed to 66·3 kcal./mole, the value we used.

The results summarised in Figs. 1—12 will now be discussed in the light of these considerations. Initially, their qualitative features are compared with observation in Tables 4 to 7, without making any allowance for departures from the calculated results. These Tables show that the conclusions derived from the calculations agree well, in broad terms, with the experimental results.

Fig. 1 shows that all the monofluorides are expected to be unstable as regards conversion into the difluoride and the element. In practice no monofluorides are known, though it is possible that CuF exists in admixture with CuF_2.[6] Fig. 1 shows that CuF is expected to be the least unstable. The graphs in Fig. 2 show that the difluorides should be stable to decomposition, though copper difluoride least so. It is not surprising, therefore, that this fluoride is the only one that shows some tendency to lose fluorine at high temperatures. This is probably a consequence of the entropy change involved in the decomposition. It is predicted that the difluorides of scandium, titanium, and vanadium should be unstable relative to $MF_3 + M$. This is in satisfactory agreement with experiment, though the position regarding vanadium difluoride in Fig. 2 is doubtful. The difluorides of chromium, manganese, and iron are obtained by the action of hydrogen fluoride on the metal, fluorine giving the trifluorides. It is perhaps surprising, from Fig. 2, that FeF_2 is not less stable. The action of fluorine on cobalt gives a mixture of di- and tri-fluoride. From the Figure, the difluoride would be expected to be just unstable relative to the trifluoride plus cobalt, but not enough to make its preparation impossible. The difluorides of nickel, copper, and zinc should be stable, and are in fact known. Fig. 2 shows that decomposition to the monofluoride is most likely to occur in the case of copper difluoride; this is a consequence of the high second ionisation potential of copper (cf. Table 2).

All the trifluorides of the elements from scandium to cobalt are known. This can be understood from Fig. 3. However this graph would suggest that nickel fluoride might also be obtainable. The figures given earlier show that the present calculations exaggerate the stability of the trifluorides and this may be the reason why nickel trifluoride has not been prepared. From Fig. 3 the existence of copper trifluoride would also be possible but in this case the error in the results for the trifluorides almost certainly means that this conclusion is unsound. The fact that zinc trifluoride is unknown can be understood from Fig. 3, this being a consequence of the high third ionisation potential of zinc.

It would be expected from Fig. 4 that all the monochlorides would be unstable relative to the dichlorides. In fact only copper monochloride is known, and that this is more readily obtained than copper monofluoride can be understood from a comparison of Figs. 1 and 4 (see earlier discussion of experimental data). This difference between CuF and CuCl is a consequence of the greater decrease in the lattice energy between copper difluoride and monofluoride than between copper dichloride and monochloride. None of the dichlorides is expected to be unstable to decomposition and, from Fig. 5, all but scandium dichloride should be stable to conversion into MCl_3 and M. In agreement with this, all the dichlorides except that of scandium are known. As pointed out above, cupric chloride has a partially

[5] Waddington, *Trans. Faraday Soc.*, 1959, **55**, 1531.
[6] Ebert and Woitinek, *Z. anorg. Chem.*, 1933, **210**, 269; Wartenberg, *ibid.*, 1939, **241**, 318.

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covalent structure, rather than a purely ionic one. This must mean that the covalent structure is more stable than the ionic one, and since the latter should be stable relative to other valency states, the covalent structure is likely to be even more so. The results in Fig. 5 would suggest that scandium dichloride though probably unstable, should be obtainable.

The trichlorides of Sc, Ti, and V should, according to Fig. 6, be known, and they are. Chromium trichloride is on the borderline, but it is not surprising that it is known.

TABLE 4. *Comparison of the calculated behaviour of the fluorides, as shown in Figs. 1—3, and the observed behaviour.*

	MF		MF_2		MF_3	
Element	Exptl.	Theory	Exptl.	Theory	Exptl.	Theory
Sc	Unknown	Unstable to $MF_2 + M$	Unknown	Just unstable to $MF_2 + M$	Known	Stable to decomp.
Ti	Unknown	,,	Unknown	,,	Known	,,
V	Unknown	,,	Unknown	Might be just stable to $MF_2 + M$	Known	,,
Cr	Unknown	,,	Known (HF + Cr at red heat)	,,	Known	,,
Mn	Unknown		Known (from Mn + HF; $MnF_2 + \frac{1}{2}F_2 \longrightarrow MnF_3$)	Just unstable to $MF_2 + M$	Known (heat $\longrightarrow MnF_2 + \frac{1}{2}F_2$)	,,
Fe	Unknown	,,	Known (from Fe + HF or red. of FeF_3)	More unstable to $MF_2 + M$	Known ($Fe + F_2$)	,,
Co	Unknown		Known ($Co + F_2 \longrightarrow CoF_2 + CoF_3$)	Just unstable to $MF_2 + M$	Known (heat $\longrightarrow CoF_2 + \frac{1}{2}F_2$)	,,
Ni	Unknown	,,	Known (very stable)	Stable to $MF_2 + M$	Unknown	,,
Cu	Doubtful	,, (but least so)	Known (at 950° $\longrightarrow$ mixt. of CuF + CuF_2)	,,	Unknown	,,
Zn	Unknown	,,	Known	,,	Unknown	Unstable to decomp.

TABLE 5. *Comparison of the calculated behaviour of the chlorides, as shown in Figs. 4—6, and the observed behaviour.*

Ele-	MCl		MCl_2		MCl_3	
ment	Exptl.	Theory	Exptl.	Theory	Exptl.	Theory
Sc	Unknown	Unstable to $MCl_2 + M$	Unknown	Border line stable to $M + MCl_3$	Known	Stable to decomp.
Ti	Unknown	,,	Known ($TiCl_3 + H_2$)	,,	Known	,,
V	Unknown		Known ($H_2 + VCl_4$ at red heat)	Stable to both	Known (HCl + V at 350°)	,,
Cr	Unknown		Known (Cr + HCl at high temps.)	,,	Known ($Cr + Cl_2$ at high temps.)	Borderline stable to decomp.
Mn	Unknown	,,	Known (HCl on Mn)		Probably known, very unstable	Unstable to decomp.
Fe	Unknown		Known (HCl on Fe)	,,	Known ($Fe + Cl_2$)	Stable to decomp.
Co	Unknown	,,	Known ($Co + Cl_2$)	,,	Doubtful	Unstable to decomp.
Ni	Unknown	,,	Known ($Ni + Cl_2$)	,,	Unknown	,,
Cu	Known	Only just unstable to $Cu + CuCl_2$	Known (covalent structure)	Just stable to decomp.	Unknown	,,
Zn	Unknown	Unstable to $ZnCl_2 + Zn$	Known	Stable to both	Unknown	,,

Manganese trichloride probably exists, but is very unstable, which can also be understood from Fig. 6. The trichloride of iron is known and is stable, as would be expected from the Fig. Cobalt trichloride would be expected to be like manganese trichloride, and its existence is in fact doubtful. The trichlorides of Ni, Cu, and Zn are unknown, as would be expected from Fig. 6.

The lower stability, in general, of the trichlorides compared with the trifluorides is a consequence of their lower lattice energies. As a result of this, for several of the elements,

FIG. 1. *The heats of reactions involving the decomposition of the compounds* MF. *(In this and the following Figs., two points are plotted for each substance where there is uncertainty regarding ionic radii. The points correspond to the extremes.)*

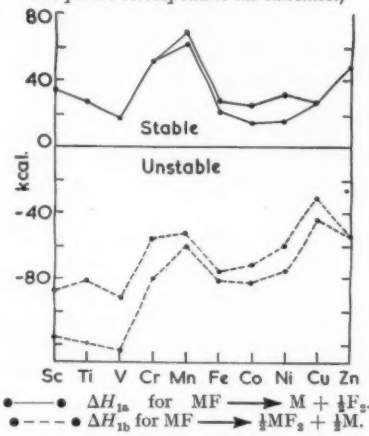


FIG. 2. *The heats of reactions involving the decomposition of the compounds* MF_2.

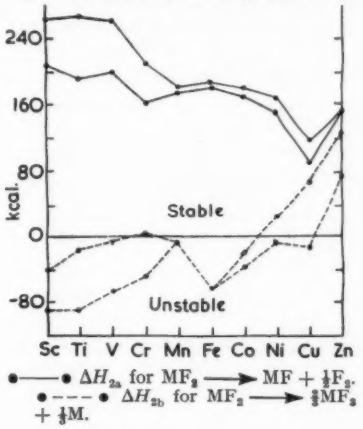


FIG. 3. *The heat of decomposition of* MF_2 *to* MF_2 *and* F_2.

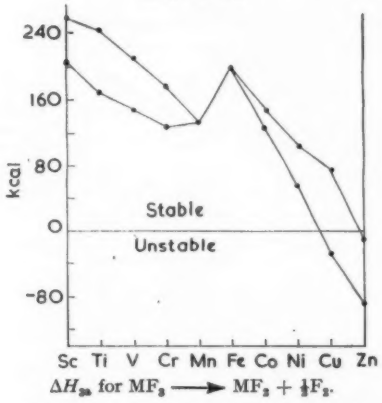


FIG. 4. *The heats of reactions involving the decomposition of the compounds* MCl.

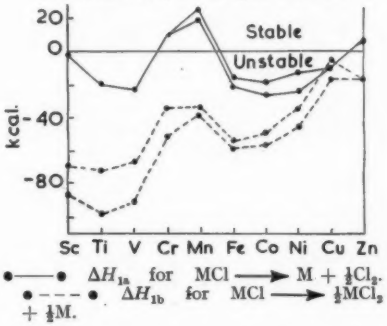


FIG. 5. *The heats of reactions involving the decomposition of the compounds* MCl_2.

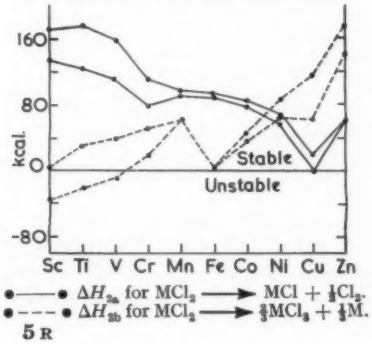
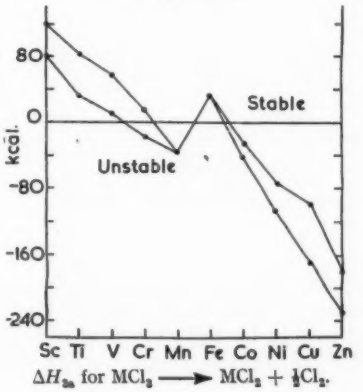


FIG. 6. *The heat of decomposition of* MCl_3 *to* MCl_2 *and* Cl_2.



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the increase in lattice energy between the dichloride and the trichloride is not sufficient to outweigh, in magnitude, the third ionisation potentials of the metals. This is only possible for Sc, Ti, V, Cr, and Fe, which have lower third ionisation potentials than Mn, Co, Ni, Cu, and Zn. The trichlorides of Ni, Cu, and Zn are unknown; these are the three metals with the highest third ionisation potentials.

TABLE 6. *Comparison of the calculated behaviour of the bromides, as shown in Figs. 7—9, and the observed behaviour.*

Element	MBr		MBr_2		MBr_3	
	Exptl.	Theory	Exptl.	Theory	Exptl.	Theory
Sc	Unknown	Unstable to M + MBr_3	Unknown	Borderline stable to Sc + $ScBr_3$	Known	Stable to decomp.
Ti	Unknown	,,	Known	Just stable to Ti + $TiBr_3$	Known	Borderline stable to decomp.
V	Unknown	,,	Known (VBr_3 + H_2)	Stable to both	Known (V + Br_2)	,,
Cr	Unknown	,,	Known	,,	Known	Unstable to decomp.
Mn	Unknown	,,	Known	,,	Unknown	,,
Fe	Unknown	Unstable to both	Known (Br_2 on Fe)	,,	Known, decomp. easily	Just unstable to decomp.
Co	Unknown	,,	Known	,,	Unknown	Unstable to decomp.
Ni	Unknown	,,	Known	,,	Unknown	,,
Cu	Known	Unstable to decomp.; borderline to Cu + $CuBr_2$	Known (covalent struct.)	Just unstable to decomp.	Unknown	,,
Zn	Unknown	Just unstable to both	Known	Stable to both	Unknown	,,

TABLE 7. *Comparison of the calculated behaviour of the iodides, as shown in Figs. 10—12, and the observed behaviour.*

Element	MI		MI_2		MI_3	
	Exptl.	Theory	Exptl.	Theory	Exptl.	Theory
Sc	Unknown	Unstable to decomp. and to M + MI_3	Unknown	Stable to decomp., just stable to ScI_3 + Sc	Known	Just stable to decomp.
Ti	Unknown	,,	Known (at 480° Ti + TiI_4)	Stable to both	Known (at 200° ⟶ TiI_2)	Unstable to decomp.
V	Unknown	,,	Known (by heating VI_3)	,,	Known (I_2 + V at 150°; at 280° ⟶ VI_3 + I_2)	,,
Cr	Unknown	,,	Known (stable to high temps.)	,,	Hydrates known, anhyd. CrI_3 said to be impossible to make	,,
Mn	Unknown	,,	Known (hydrates lose I_2 at 80°)	,,	Unknown	,,
Fe	Unknown	,,	Known (I_2 + Fe)	Stable to FeI_2 + Fe, and to decomp. to FeI + I_2 (but just unstable to Fe + I_2)	Unknown	,,
Co	Unknown	,,	Known (HI + Co; at 540°, decomp.)	,,	Unknown	,,
Ni	Unknown	,,	Known (Ni + I_2)	Borderline stable to decomp. to NiI + I_2	Unknown	,,
Cu	Known	Unstable to decomp. but just stable to Cu + CuI_2	Very unstable (⟶ CuI + I_2)	Unstable to decomp.	Unknown	,,
Zn	Unknown	Unstable to both	Known	Borderline stable to decomp. to ZnI + I_2	Unknown	,,

The non-existence of almost all the monobromides is in agreement with Fig. 7. The existence of copper monobromide would, from the Fig., be a little surprising, as it is predicted to be slightly unstable to decomposition, but, as we have seen above, its existence can be understood, because of the increased covalency of the binding in the

crystal. The situation with the dibromide (Fig. 8) is very similar to that of the dichlorides (Fig. 5), and the experimental situation is also very similar. The stability of copper dibromide can also be understood in terms of covalency in the binding (see Figs. given earlier).

FIG. 7. *The heats of reactions involving the decomposition of the compounds MBr.*

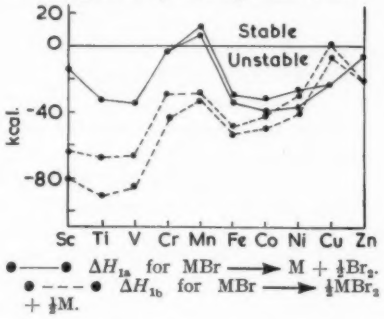


FIG. 8. *The heats of reactions involving the decomposition of the compounds* MBr_2.

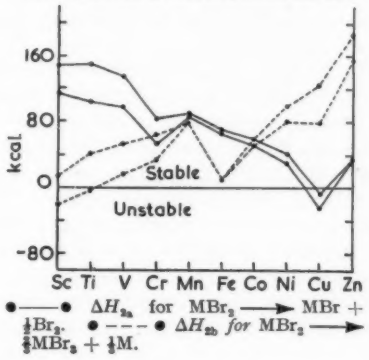


FIG. 9. *The heat of decomposition of* MBr_3 *to* MBr_2 *and* Br_2.

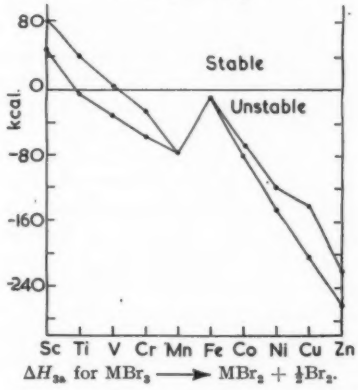


FIG. 10. *The heats of reactions involving the decomposition of the compounds* MI.

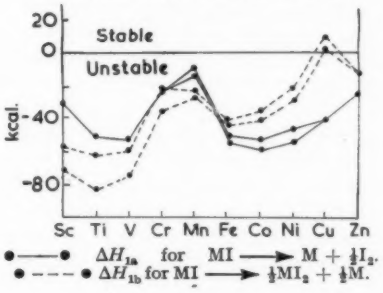


FIG. 11. *The heats of reactions involving the decomposition of the compounds* MI_2.

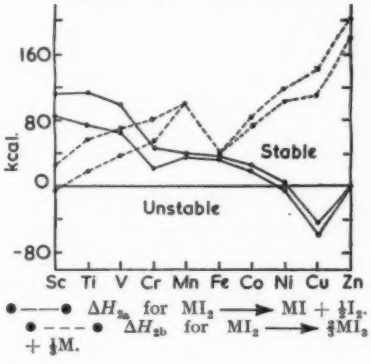
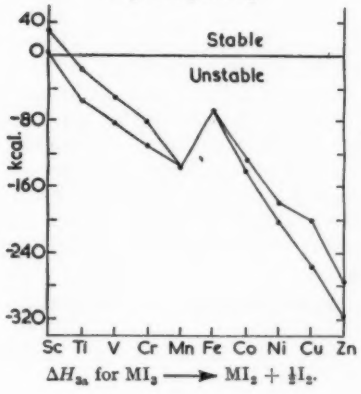


FIG. 12. *The heat of decomposition of* MI_3 *to* MI_2 *and* I_2.



Of the tribromides, those of Sc, Ti, V, Cr, and Fe are known, the others are not. This is quite consistent with the results presented in Fig. 9 (see also Table 3), and it is interesting that the calculations predict that manganese tribromide is likely to be non-existent (cf. $MnCl_3$). In those compounds consisting of a largish anion and a highly charged cation, there will be some covalent character in the binding, so that this is likely to contribute to the existence of the tribromides of chromium and iron. The latter is said to decompose easily, as would be expected from Fig. 9. The tribromides can be discussed in the same terms as the trichlorides.

Fig. 10 shows that all the monoiodides would be expected to be unstable to dissociation, and that all except copper monoiodide would be unstable relative to MI_2 and M. In fact only copper monoiodide is known. Undoubtedly, the additional stability of the CuI lattice (zinc blende) is achieved by the adoption of some covalent character in the binding, which will enhance its stability relative to decomposition.

Of the di-iodides, Fig. 11 suggests that all except copper di-iodide should be stable. In fact all are known except scandium di-iodide (copper di-iodide is very unstable), so that the calculated behaviour agrees fairly well with observations. The stability of the di-iodides of Fe, Co, Ni, and Zn, despite the fact that the calculations suggest that they should be unstable to decomposition to the metal and iodine, must be due to some covalent character in the bonding in their crystals. FeI_2 and CoI_2 have the CdI_2 layer structure, and NiI_2 the $CdCl_2$ structure, which undoubtedly are covalent in character.

Of the tri-iodides, all except that of scandium would be expected to be unstable. However, in addition to ScI_3, TiI_3 and VI_3 are known, although both decompose easily in the range 200—300°. This can be understood from Fig. 12, particularly if it is supposed that the iodides are not purely ionic, because it would be expected that there would be more covalent character in the tri-iodides than in the di-iodides (Fajans's rules), so that the relative stabilities of the tri-iodides would be increased (see above). The absence of the tri-iodides of the later members is to be expected.

It is clear that these quite simple calculations do account for the occurrence of these halides rather satisfactorily. Take the trihalides as an example; it is shown clearly how the greater lattice energy of the fluorides favours the existence of the trifluorides. On the other hand, the low lattice energies of the tri-iodides result in very few of these being obtainable, and most of those that are have low stability. The chlorides and bromides are intermediate, and calculations bring out clearly the low stabilities of $MnCl_3$ and $MnBr_3$ relative to $CrCl_3$ and $CrBr_3$, and $FeCl_3$ and $FeBr_3$. This is a consequence of the high third ionisation potential of manganese, the reason for this being that in Mn^{2+}, the *d*-shell is half-filled, and hence stable. There are many other effects that can be explained in similar terms, by examining the lattice energies, ionisation potentials, etc.

General Conclusions.—Kapustinskii's very simple formula provides a most useful means of estimating and comparing the stabilities of a number of solid inorganic halides. However, comparison of the calculated heats of formation with observed values shows that for structures in which there may be more covalent binding than in the chlorides (*e.g.*, the bromides and iodides), the lattice energy is underestimated by Kapustinskii's formula. For the fluorides this situation appears to be reversed, the formula exaggerating the lattice energies. When stabilities are considered some allowance must be made for these effects though, because differences are involved, the discrepancies in the heats of reaction may not be as great as those in the lattice energies.

The calculations suggest that it might be worthwhile to investigate the possibility of preparing such compounds as scandium dibromide and di-iodide and perhaps nickel trifluoride.

INORGANIC CHEMISTRY LABORATORY, OXFORD. [*Received, March 3rd, 1960.*]

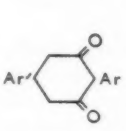
651. *Cyclohexane-1,3-diones. Part VI.*[1] *Structural Requirements for the Displacement of the Alkoxyl by the Cyano-group in the Enol Ethers of Cyclic β-Diketones.*

By B. E. Betts and W. Davey.

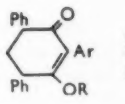
A series of β-diketones have been prepared and converted into the corresponding enol ethers. The replacement of the alkoxyl group by a cyano-group by treatment with acetone cyanohydrin has been studied, and the reaction shown to be restricted to the alkyl enol ethers of 2-arylcycloalkane-1,3-diones.

The structural requirements for the reaction of enol ethers of cyclohexane-1,3-diones with acetone cyanohydrin, reported in Parts II [2] and V,[1] have now been elucidated.

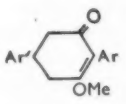
Cyclohexane-1,3-dione (Ia) and its 5-phenyl- (Ib),[3] 4,6-diphenyl- (IIa),[4] and 5-styryl- (Ic) [5] derivatives were converted into the corresponding methyl enol ethers with diazomethane but all four enol ethers were recovered unchanged from attempted reactions with acetone cyanohydrin. When 3-methoxy-5-phenylcyclohex-2-en-1-one (IIIa) was used, a small quantity of 2,2,5,5-tetramethyl-4-oxazolidone [6,7] was isolated as by-product. The inability of these enol ethers to undergo exchange, in contrast to 3-methoxy-2,5-diphenylcyclohex-2-en-1-one (IIIb), suggests that a phenyl group or possibly some other substituent in the 2-position is a prerequisite for reaction.



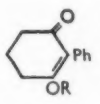
(Ia); Ar = Ar′ = H
(Ib); Ar = H, Ar′ = Ph
(Ic); Ar = H, Ar′ = CHPh:CH
(Id); Ar = 4-MeO·C_6H_4, Ar′ = H
(Ie); Ar = 4-O_2N·C_6H_4, Ar′ = H
(If); Ar = 2,4-$(O_2N)_2C_6H_3$, Ar′ = H
(Ig); Ar = 4-NC_6H_4, Ar′ = H
(Ih); Ar = Pr^i, Ar′ = Ph



(IIa); Ar = R = H
(IIb); Ar = Ph, R = H
(IIc; Ar = Ph, R = Me



(IIIa); Ar = H, Ar′ = Ph
(IIIb); Ar = Ar′ = Ph
(IIIc); Ar = 4-MeO·C_6H_4, Ar′ = H
(IIId); Ar = 2,4-$(O_2N)_2C_6H_3$, Ar′ = H
(IIIe); Ar = Pr^i, Ar′ = Ph
(IIIf); Ar = H, Ar′ = CHPh:CH



(IVa); R = H
(IVb); R = Me
(IVc); R = Et
(IVd); R = CH_2Ph
(IVe); R = Bu^t

2-Phenylcyclohexane-1,3-dione (IVa) was converted into the methyl enol ether (IVb) by Born, Pappo, and Szmuskovicz's method.[8] The ethyl enol ether (IVc) was obtained by treatment of the sodio-derivative of the dione (IVa) with ethyl iodide, since reaction of the dione with ethyl orthoformate gave unchanged material. The benzyl enol ether (IVd) was similarly prepared from the potassio-derivative and benzyl chloride. The dione (IVa) with phosphorus trichloride gave 3-chloro-2-phenylcyclohex-2-en-1-one (V), but an attempt to convert this into the t-butyl enol ether (IVe) by treatment with potassium t-butoxide gave an unidentified compound, $C_{24}H_{20}O_2$.

All three enol ethers (IVb), (IVc), and (IVd) underwent exchange with acetone cyanohydrin at room temperature to give 3-cyano-2-phenylcyclohex-2-en-1-one (VIa) in similar yield, thus showing the necessity for a 2-substituent and indicating that the nature of the alkoxyl group had little if any effect on the displacement. Treatment of this cyano-ketone (VIa) with more acetone cyanohydrin at 90° afforded a small quantity of material which,

[1] Part V, *J.*, 1961, 1683.
[2] Part II, Ames and Davey, *J.*, 1957, 3480.
[3] Vorlander, *Ber.*, 1894, **27**, 2053.
[4] Ames and Davey, *J.*, 1958, 1794.
[5] Vorlander, *Annalen*, 1896, **294**, 273.
[6] Ultee, *Rec. Trav. chim.*, 1909, **28**, 259.
[7] Snyder and Elston, *J. Amer. Chem. Soc.*, 1954, **76**, 3039.
[8] Born, Pappo, and Szmuskovicz, *J.*, 1953, 1779.

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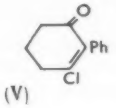
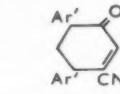
by analogy with the reactions of 3-methoxy-2,5-diphenylcyclohex-2-en-1-one (IIIb),[1] is considered to be 1,5-dicyano-8-phenyl-6-azabicyclo[3,2,1]octan-7-one (VIIa).

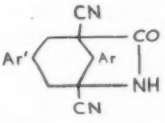
The effect of the substituent at position 2 was next investigated. 2-*p*-Methoxyphenylcyclohexane-1,3-dione (Id) was prepared as for the 2-phenyl-dione (IVa), but similar preparation of the 2-*p*-nitro-compound (Ie) was not possible since the initial condensation of *p*-nitrobenzyl cyanide with diethyl glutarate could not be achieved. An attempt to prepare the intermediate keto-acid (VIII) by conversion of propane-1,1,3-tricarboxylic acid (IXa) [9,10] into the tetrahydropyranyl ester (IXb) by Bowman and Fordham's procedure,[11] followed by condensation of the sodio-derivative of this ester with *p*-nitrophenylacetyl chloride, gave only *p*-nitrophenylacetic acid. Attempts to prepare the dione (Id) by direct arylation [12] of cyclohexane-1,3-dione (Ia) with *p*-fluoronitrobenzene were also unsuccessful. Sodium ethoxide-catalysed reaction of cyclohexane-1,3-dione (Ia) with 1-fluoro-2,4-dinitrobenzene, however, gave 2-(2,4-dinitrophenyl)cyclohexane-1,3-dione



(V)



(VIa); Ar = Ph, Ar′ = H
(VIb); Ar = 4-MeO·C_6H_4, Ar′ = H
(VIc); Ar = 2,4-$(O_2N)_2C_6H_3$, Ar′ = H
(VId); Ar = Ar′ = Ph



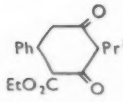
(VIIa); Ar = Ph, Ar′ = H
(VIIb); Ar = 2,4-$(O_2N)_2C_6H_3$, Ar′ = H
(VIIc); Ar = Ar′ = Ph

(If) in 25% yield. Preparation of 2-4′-pyridylcyclohexane-1,3-dione (Ig) as previously described [8] required 4-cyanomethylpyridine as starting material. This nitrile was prepared [13] from 4-chloromethylpyridinium chloride and potassium cyanide; Itai and Ogura's method [14] gave only unchanged material. Condensation of this nitrile with diethyl glutarate furnished ethyl 6-cyano-5-oxo-6-4′-pyridylhexanoate (Xa), which could not be hydrolysed to the keto-acid (Xb). 2-Isopropyl-5-phenylcyclohexane-1,3-dione (Ih) was prepared by Michael condensation of diethyl malonate with 5-methyl-1-phenylhex-1-en-3-one (prepared by Cason's method [15]) and subsequent hydrolysis of the dioxo-ester (XI). 5,5-Dimethyl-2-nitrocyclohexane-1,3-dione (XIIa) was prepared as described by

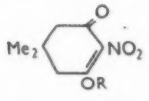
4-O_2N·C_6H_4·CH_2·CO·$[CH_2]_3$·CO_2H (VIII)

$(RO_2C)_2CH·CH_2·CH_2·CO_2R$ (IXa); R = H
(IXb); R = Tetrahydropyranyl

4-NC_5H_4·CHR′·CO·$[CH_2]_3$·CO_2R (Xa); R = Et, R′ = CN
(Xb); R = R′ = H



(XI)



(XIIa); R = H
(XIIb); R = Me

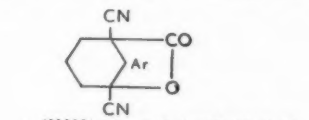
Eistert, Elias, Kosch, and Wollheim.[16] Sodium ethoxide-catalysed condensation of ethyl atropate [17] with dibenzyl ketone afforded 2,4,6-triphenylcyclohexane-1,3-dione (IIb).

All these diones were converted into the corresponding methyl enol ethers with diazomethane and the exchange studied. 3-Methoxy-2-*p*-methoxyphenylcyclohex-2-en-1-one

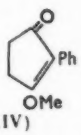
[9] Bischoff, *Annalen*, 1882, **214**, 53.
[10] Fredga, *Arkiv Kemi, Min., Geol.*, 1946, *B*, **23**, No. 2, 5.
[11] Bowman and Fordham, *J.*, 1952, 3947.
[12] Stetter, *Angew. Chem.*, 1955, **67**, 769.
[13] Mosher and Tessieri, *J. Amer. Chem. Soc.*, 1951, **73**, 4925.
[14] Itai and Ogura, *J. Pharm. Soc. Japan*, 1955, **75**, 296; *Chem. Abs.*, 1956, **50**, 1810.
[15] Cason, *J. Amer. Chem. Soc.*, 1946, **68**, 2078.
[16] Eistert, Elias, Kosch, and Wollheim, *Chem. Ber.*, 1959, **92**, 130.
[17] Schinz and Hinder, *Helv. Chim. Acta*, 1947, **30**, 1349.

(IIIc) with acetone cyanohydrin in the presence of triethylamine gave 70% of 3-cyano-2-*p*-methoxyphenylcyclohex-2-en-1-one (VIb) at room temperature and 76% of the same product at 90°. With methanolic potassium hydroxide as catalyst a 76% yield of the cyano-ketone (VIb) was isolated and 18% of the dione (Id) was recovered. With methanol as solvent the yield of (VIb) was only 20%. None of the expected cyano-ketone (VIc) could be isolated from reaction of 2-(2,4-dinitrophenyl)-3-methoxycyclohex-2-en-1-one (IIId) with acetone cyanohydrin at room temperature or at 90° by using triethylamine or methanolic potassium hydroxide as catalyst. In all cases the product was 1,5-dicyano-8-(2,4-dinitrophenyl)-6-azabicyclo[3,2,1]octan-7-one (VIIb), an assignment supported by the infrared spectrum.[18] Unlike the diphenylazabicyclo-octanone (VIIc),[1] this product was not converted into the corresponding cyano-ketone (VIc) by hydrochloric and acetic acids. The sole product was thought to have the structure (XIII). Both 2-isopropyl-3-methoxy-5-phenylcyclohex-2-en-1-one (IIIe) and 3-methoxy-5,5-dimethyl-2-nitrocyclohex-2-en-1-one (XIIb) were unaffected by treatment with acetone cyanohydrin. The lack of reactivity of the nitro-enol ether (XIIb), in contrast to that of the dinitrophenyl compound (IIId), suggests that an electron-attracting group attached directly to the cyclohexane ring does not exert sufficient influence to facilitate the exchange. These results indicate that the 2-aryl group is essential for the reaction and that this effect is due mainly to electronic rather than steric factors. In spite of the steric hindrance expected from the additional phenyl groups, 3-methoxy-2,4,6-triphenylcyclohex-2-en-1-one (IIc) and acetone cyanohydrin reacted at room temperature to yield 70% of 3-cyano-2,4,6-triphenylcyclohex-2-en-1-one (VId).

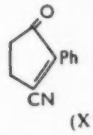
Attention was next turned to whether the exchange was restricted to cyclohexane derivatives. 3-Methoxy-2-phenylcyclopent-2-en-1-one (XIV) was prepared as for the corresponding cyclohexenone (IVb). Base-catalysed reaction with acetone cyanohydrin at room temperature or at 90° gave 3-cyano-2-phenylcyclopent-2-en-1-one (XV) as the sole product. 3-Phenylpentane-2,4-dione (XVIa) was prepared by acetylation of benzyl



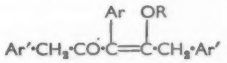
(XIII); Ar = 2,4-$(O_2N)_2C_6H_3$



(XIV)



(XV)



(XVIa); Ar = Ph, Ar′ = R = H
(XVIb); Ar = Ar′ = Ph, R = H
(XVIc); Ar = Ar′ = Ph, R = Me
(XVId); Ar = 2,4-$(O_2N)_2C_6H_3$, Ar′ = R = H
(XVIe); Ar = 2,4-$(O_2N)_2C_6H_3$, Ar′ = H, R = Me

methyl ketone[19] *as the Claisen condensation of this ketone with ethyl acetate*[20] gave a negligible yield of the dione, and other methods failed. Condensation of ethyl phenylacetate with dibenzyl ketone afforded 1,3,5-triphenylpentane-2,4-dione (XVIb) which was converted into the enol ether (XVIc). This was recovered from treatment with acetone cyanohydrin. Arylation of pentane-2,4-dione with 1-fluoro-2,4-dinitrobenzene gave the required dione (XVId) which, with diazomethane, afforded 3-(2,4-dinitrophenyl)-4-methoxypent-3-en-2-one (XVIe). From treatment with acetone cyanohydrin in boiling methanol, this enol ether (XVIe) was recovered but in the absence of methanol no crystalline material could be isolated. The failure of 2-methoxy-1,3,5-triphenyl- (XVIc) and 3-(2,4-dinitrophenyl)-4-methoxypent-3-en-2-one (XVIe) to exchange in contrast to the corresponding cyclic compounds (IIc) and (IIId) suggests that a cyclic system is necessary.

[18] Bellamy, "Infrared Spectra of Complex Molecules," Methuen, London, 1958, (*a*), p. 205, (*b*) p. 186.
[19] Hauser and Manyik, *J. Org. Chem.*, 1953, **18**, 589.
[20] Morgan, Drew, and Porter, *Ber.*, 1925, **58**, 333.

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To confirm that the exchange was restricted to enol ethers of β-diketones, the synthesis of 2-methoxy-1-phenylcyclohex-1-ene was attempted but could not be achieved. It was hoped that dehydrochlorination and etherification [21] of 1,1-dichloro-2-phenylcyclohexane would afford the cyclohexene but reaction of 2-phenylcyclohexanone with phosphorus pentachloride yielded 2-phenylcyclohex-2-en-1-one. Also, although the action of phenylmagnesium bromide on 2-methoxycyclohexanone [22] gave 2-methoxy-1-phenylcyclohexan-1-ol, yet attempted dehydration of this alcohol with phosphorus pentoxide gave 2-phenylcyclohexanone, and heating it with anhydrous copper sulphate in dry xylene gave a complex mixture of products.

From these results, it is apparent that the reaction of enol ethers of β-diketones with acetone cyanohydrin resulting in the displacement of an alkoxyl group by a cyano-group is restricted to the alkyl enol ethers of 2-arylcycloalkane-1,3-diones.

It is noteworthy that those enol ethers (IVb), (IVc), (IVd), (IIIc), (IIId), and (IIc) which underwent exchange showed two absorption maxima at 228—230 and near 270 mμ, the latter band being the stronger; enol ethers which did not react had only one absorption maximum in the 260-mμ region.

Experimental

" Light petroleum " refers to the fraction, b. p. 60—80°.

Preparation of β-Diketones.—*2-Phenylcyclohexane-1,3-dione* (IVa). The dione [8] crystallised from benzene as the *hemihydrate*, plates, m. p. 158° (Found, after drying at 110°/0·1 mm.: C, 73·5; H, 6·3. $C_{12}H_{12}O_2,\frac{1}{2}H_2O$ requires C, 73·1; H, 6·6%). Born *et al.*[8] report m. p. 160—161° for the anhydrous material.

2-p-*Methoxyphenylcyclohexane-1,3-dione* (Id). The dione was prepared from *p*-methoxybenzyl cyanide and diethyl glutarate by the procedure employed for the foregoing compound. *Ethyl 6-cyano-6-p-methoxyphenyl-5-oxohexanoate* (48%), obtained as a yellow oil, b. p. 190—191°/0·4 mm. (Found: C, 66·2; H, 6·8; N, 4·6. $C_{16}H_{19}NO_4$ requires C, 66·4; H, 6·6; N, 4·8%), was hydrolysed to *6-p-methoxyphenyl-5-oxohexanoic acid* (85%), needles, m. p. 86°, from light petroleum (Found: C, 66·1; H, 7·1. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%). The corresponding *oxime* formed prisms, m. p. 122°, from ethyl acetate–light petroleum (Found: C, 61·9; H, 6·5; N, 5·7. $C_{12}H_{17}NO_4$ requires C, 62·1; H, 6·8; N, 5·6%). *The ethyl ester*, b. p. 158—160°/0·3 mm., which crystallised quantitatively from ether as plates, m. p. 43—44° (Found: C, 67·8; H, 7·5. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·6%), was cyclised to 2-p-*methoxyphenylcyclohexane-1,3-dione* (79%), plates, m. p. 175°, from benzene (Found: C, 71·2; H, 6·7. $C_{13}H_{14}O_3$ requires C, 71·5; H, 6·5%).

2-*Phenylcyclopentane-1,3-dione*. The dione was prepared from benzyl cyanide and diethyl succinate by the procedure used for the cyclohexane analogue. *Ethyl 5-cyano-4-oxo-5-phenylpentanoate* (47%), b. p. 160—162°/0·5 mm., m. p. 152° (from benzene–light petroleum) (Found: C, 69·1; H, 5·9; N, 5·4. $C_{14}H_{15}NO_3$ requires C, 68·6; H, 6·2; N, 5·7%), was converted into ethyl 4-oxo-5-phenylpentanoate (79%), b. p. 121—122°/0·3 mm. (Found: C, 70·5; H, 7·2. Calc. for $C_{13}H_{16}O_3$: C, 70·9; H, 7·3%) (Stefanova [23] gave b. p. 169—170°/20 mm.). Cyclisation of the latter ester gave the dione, needles, m. p. (inserted at 200°) 247°, from acetic acid (Found: C, 75·9; H, 5·7. Calc. for $C_{11}H_{10}O_2$: C, 75·8; H, 5·8%). Erskola [24] records m. p. 233—234°.

2-(2,4-*Dinitrophenyl*)*cyclohexane-1,3-dione* (If). Cyclohexane-1,3-dione (5·6 g.), followed by 1-fluoro-2,4-dinitrobenzene (10·2 g.), was added to a solution from sodium (1·1 g.) and dry ethanol (40 c.c.), and the mixture was refluxed for 3 hr., then poured into 2N-sodium hydroxide, washed with ether, acidified, and re-extracted with ether. Evaporation of the dried extract and crystallisation from ethyl acetate gave the required *dione* (25%), yellow plates, m. p. 252° (Found: C, 51·6; H, 3·8; N, 10·0. $C_{12}H_{10}N_2O_6$ requires C, 51·8; H, 3·9; N, 10·1%). Concentration of the original ether washings afforded 1-ethoxy-2,4-dinitrobenzene (1·9 g.), m. p. 85·5° (lit., m. p. 85—86°). When potassium hydroxide (2·8 g.) in methanol (12 c.c.) and water (8 c.c.) was used as the condensing agent, the yield of the required dione was only 9%, and

[21] Markownikoff, *Annalen*, 1903, **327**, 69.
[22] Bergmann and Gierth, *Annalen*, 1926, **448**, 64.
[23] Stefanova, *Annuaire Univ. Sofia, Faculte phys.-maths.*, 1943—4, **40**, Livre 2, 147.
[24] Erskola, *Suomen Kem.*, 1938, **11**, *B*, 9; *Chem. Abs.*, 1938, **32**, 3359.

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concentration of the mother-liquor furnished 2,4-dinitrophenol (6·8 g.), m. p. and mixed m. p. 114°, and unchanged cyclohexane-1,3-dione (0·9 g.), m. p. and mixed m. p. 104°.

5-Methyl-1-phenylhex-1-en-3-one. Condensation of cinnamoyl chloride with di-isobutylcadmium according to Cason's method [15] gave the hexenone (49%), b. p. 125—129°/2·0 mm., n_D^{20} 1·558 (Found: C, 82·4; H, 8·7. Calc. for $C_{13}H_{16}O$: C, 82·9; H, 8·6%). Gheorghiu and Arwentiew [25] record b. p. 179—183°/32 mm., n_D^{20} 1·557. The *2,4-dinitrophenylhydrazone*, orange prisms from ethyl acetate, had m. p. 176° (Found: C, 62·2; H, 5·8; N, 14·8. $C_{19}H_{20}N_4O_4$ requires C, 61·9; H, 5·5; N, 15·2%). *The semicarbazone formed needles, m. p. 167°, from* ethanol (Found: C, 68·6; H, 7·8; N, 17·2. Calc. for $C_{14}H_{19}N_3O$: C, 68·6; H, 7·8; N, 17·1%). Gheorghiu and Arwentiew [25] give m. p. 167°.

Ethyl 3-isopropyl-2,4-dioxo-6-phenylcyclohexanecarboxylate. To sodium (1·2 g.) in dry ethanol (30 c.c.) was added diethyl malonate (8·5 g.) followed by 5-methyl-1-phenylhex-1-en-3-one (10·0 g.), and the mixture was refluxed for 3·5 hr. The ethanol was evaporated under reduced pressure, and the residue diluted with water. The aqueous suspension was washed with ether, acidified and then extracted with ether. Concentration of the dried extract afforded the *dioxo-ester* (12·0 g.), needles, m. p. 136°, from benzene–light petroleum (Found: C, 71·1; H, 7·2. $C_{18}H_{22}O_4$ requires C, 71·5; H, 7·3%).

2-Isopropyl-5-phenylcyclohexane-1,3-dione (Ih). The preceding ester (12·0 g.) was refluxed for 9 hr. with sodium carbonate (25·0 g.) in water (70 c.c.). The solution was acidified and then boiled to give a quantitative yield of the dione, needles, m. p. 191°, from ethanol. Desai [26] records m. p. 190°.

5,5-Dimethyl-2-nitrocyclohexane-1,3-dione (XIIa) was obtained as described by Eistert, Elias, Kosch, and Wollheim.[16] It was essential to keep the reaction mixture below room temperature during the removal of the ether to avoid violent decomposition of the product.

2,4,6-Triphenylcyclohexane-1,3-dione (IIb). Dibenzyl ketone (21·0 g., 1 mol.) and ethyl atropate (18·0 g., 1 mol.) [17] were successively added to sodium (4·6 g., 2 g.-atoms) in dry ethanol (100 c.c.), and the mixture was refluxed for 3 hr. The solution was diluted with water and washed with ether. Acidification of the aqueous fraction furnished *2,4,6-triphenylcyclohexane-1,3-dione* (27%), needles, m. p. 215°, from methanol (Found: C, 84·5; H, 5·9. $C_{24}H_{20}O_2$ requires C, 84·7; H, 5·9%). If only 1 g.-atom of sodium was used the yield of dione was only 14%.

1,3,5-Triphenylpentane-2,4-dione (XVIb). Sodium (3·5 g.) was slowly added to dibenzyl ketone (31·5 g.) and ethyl phenylacetate (24·6 g.). When the initial reaction had subsided the mixture was stirred on a hot-water bath for 3·5 hr. and then dissolved in water and washed with ether. The sodium salt was decomposed by addition of solid carbon dioxide, and the *dione* (1·7 g.) thus obtained recrystallised from ethyl acetate–light petroleum as needles, m. p. 212° (Found: C, 84·2; H, 6·0. $C_{23}H_{20}O_2$ requires C, 84·1; H, 6·1%).

3-(2,4-Dinitrophenyl)pentane-2,4-dione (XVId). The *dione*, prepared from pentane-2,4-dione and 1-fluoro-2,4-dinitrobenzene in the same manner as 2-(2,4-dinitrophenyl)cyclohexane-1,3-dione, crystallised as plates, m. p. 122°, from ethyl acetate–light petroleum (Found: C, 49·8; H, 3·9; N, 10·4. $C_{11}H_{10}N_2O_6$ requires C, 49·6; H, 3·8; N, 10·5%).

Enol Ethers.—The methyl enol ethers listed in Table 1 were obtained by treatment of a methanolic suspension of the appropriate dione with a slight excess of ethereal diazomethane, and were isolated by evaporation of the mixture.

3-Ethoxy-2-phenylcyclohex-2-en-1-one (IVc). To sodium (0·5 g.) in dry ethanol (20 c.c.) were added 2-phenylcyclohexane-1,3-dione (3·8 g.) and ethyl iodide (3·1 g.), and the mixture was refluxed for 2 hr., then concentrated, diluted with water, and extracted with ether. The extract was washed with 5% aqueous sodium hydroxide to remove any dione and then concentrated to yield 3-ethoxy-2-phenylcyclohex-2-en-1-one (2·9 g.), needles, m. p. 96°, from light petroleum (Found: C, 77·4; H, 7·3. Calc. for $C_{14}H_{16}O_2$: C, 77·7; H, 7·5%). Born *et al.*[3] report m. p. 102°.

3-Benzyloxy-2-phenylcyclohex-2-en-1-one (IVd). 2-Phenylcyclohexane-1,3-dione (4·0 g.) and benzyl chloride (2·7 g.) were successively added to potassium (0·9 g.) in dry t-butyl alcohol (30 c.c.), and the mixture was refluxed for 6 hr., then concentrated, diluted with water, and extracted with ether. Distillation of the extract gave an oil which on trituration with ether afforded *3-benzyloxy-2-phenylcyclohex-2-en-1-one* (2·1 g., 36%), prisms, m. p. 70—71°, from light petroleum (Found: C, 81·7; H, 6·5. $C_{19}H_{18}O_2$ requires C, 82·0; H, 6·5%). When sodium

[25] Gheorghiu and Arwentiew, *J. prakt. Chem.*, 1928, **118**, 295.
[26] Desai, *J.*, 1932, 1079.

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in ethanol was used in place of potassium in t-butyl alcohol the yield of the enol ether was only 17%.

Exchange Reactions with Acetone Cyanohydrin.—General procedure. (*a*) The enol ether was dissolved in the minimum volume of redistilled acetone cyanohydrin at room temperature, 13% methanolic potassium hydroxide (0·1 c.c./10 c.c. of acetone cyanohydrin) was added, and the

TABLE 1. *Methyl enol ethers.*

Compound	Form [a]	M. p.	Yield (%)	Formula	Found (%) C	H	N	OMe	Required (%) C	H	N	OMe
IIc	Plates [d]	171°	98	$C_{25}H_{22}O_2$	84·2	6·4	—	10·2	84·7	6·3	—	8·8
IIIc	Plates	112	92	$C_{14}H_{16}O_2$	71·9	7·0	—	—	72·4	6·9	—	—
IIId	Yellow prisms [e]	173	97	$C_{13}H_{12}N_2O_6$	53·8	4·1	9·6	—	53·4	4·1	9·6	—
IIIe	Prisms [a]	73	67	$C_{16}H_{20}O_2$	79·1	8·5	—	—	78·7	8·3	—	—
IIIf	Needles [a]	94	83	$C_{15}H_{16}O_2$	79·1	7·1	—	—	79·0	7·1	—	—
IVb	Prisms [b]	122—123 †	87	$C_{13}H_{14}O_2$	77·4	6·9	—	—	77·2	7·0	—	—
XIIb	Plates	130	65	$C_9H_{13}NO_4$	54·3	6·6	7·0	—	54·3	6·6	7·0	—
XIV	Prisms	98	98	$C_{12}H_{12}O_2$	76·6	6·4	—	—	76·6	6·4	—	—
XVIc	Needles	197—198	80	$C_{24}H_{22}O_2$	84·0	6·3	—	9·3	84·2	6·5	—	9·1
XVIe	Needles	100	90	$C_{11}H_{10}N_2O_6$	51·7	4·3	9·8	—	51·4	4·3	10·0	—

[a] From benzene–light petroleum unless otherwise stated: [c] from light petroleum; [b] from benzene; [e] from ethyl acetate; [d] from MeOH.

† Born, Pappo, and Szmuskovicz [a] give m. p. 96—98°.

mixture set aside overnight. The solution was poured into water and acidified (Congo Red), and the product filtered off. (*b*) The procedure was the same as in (*a*) except that triethylamine (0·05 c.c./10 c.c. of acetone cyanohydrin) was used as catalyst. (*c*) Triethylamine (0·05 c.c./10 c.c. of acetone cyanohydrin) was added to a solution of the enol ether in the minimum volume of acetone cyanohydrin, and the mixture heated at 80—90° for 45 min., then cooled, poured into water, and acidified (Congo Red), and the product was filtered off. The products thus obtained are listed in Table 2.

TABLE 2. *Products from exchange reactions with acetone cyanohydrin*

Starting material [a]	Product	Yield (%)	Form †	M. p.	Formula	Found (%) C	H	N	Required (%) C	H	N
IVb [a,b]	VIa [d]	37									
IVc [a,b]	VIa	30—37	Needles [d]	118°	$C_{13}H_{11}NO$	79·3	5·7	6·9	79·2	5·6	7·1
IVd [a,b]	VIa	30—40									
VIa [c]	VIIa	10	Needles	170	$C_{15}H_{13}N_3O$	71·3	5·3	16·7	71·7	5·2	16·7
IIIc [a]	VIb [1]	76	Needles [e]	93	$C_{14}H_{13}NO_2$	73·6	5·6	6·4	74·0	5·8	6·2
IIIc [b,c]	VIb [2,3]	71—76									
IIId [a,b]	VIIb [5]	25	Prisms	215	$C_{15}H_{11}N_5O_5$	52·8	3·2	20·7	52·8	3·2	20·5
IIId [c]	VIIb	13									
XIV [a,b,c]	XV	76	Needles [f]	112	$C_{12}H_9NO$	78·2	5·0	7·7	78·7	5·0	7·6
IIc [a,b]	VId	65	Prisms [c]	151	$C_{25}H_{19}NO$	85·9	5·7	3·8	85·9	5·5	4·0

[a] For method used see general procedures (*a*), (*b*), and (*c*).

† From ethyl acetate unless otherwise stated: [d] from benzene–light petroleum; [c] from ethyl acetate–light petroleum; [f] from light petroleum.

[1] 18% of the dione (Id), m. p. and mixed m. p. 175°, was also isolated. [2] The derived *oxime* formed needles, m. p. 212°, from ethanol (Found: C, 69·1; H, 6·2; N, 11·4. $C_{14}H_{14}N_2O_2$ requires C 69·4; H, 5·8; N, 11·6%). [3] Addition of methanol as solvent reduced the yield to 20%. [4] Infrared spectrum (KBr disc), bands at 2210 (conjugated C≡N), 1675 (αβ-unsaturated C=O), 765 and 702 cm.$^{-1}$ (phenyl system). [5] Infrared spectrum (KBr disc), bands at 3303 (NH), 2247 (C≡N), 1721 (C=O, fused ring γ-lactam), 1538 and 1358 cm.$^{-1}$ (NO_2).

Treatment of 1,5-*Dicyano*-8-(2,4-*dinitrophenyl*)-6-*azabicyclo*[3,2,1]*octan*-7-*one* (VIIb) *with Acid.*—The azabicyclo-octanone (1·4 g.) in acetic acid (50 c.c.), concentrated hydrochloric acid (4 c.c.), and water (4 c.c.) was refluxed for 12 hr. The solvents were evaporated *in vacuo* and the residue was diluted with water. The solid was filtered off and recrystallised from ethyl acetate to give a *substance*, prisms, m. p. 244° [Found: C, 52·0; H, 3·1; N, 15·5; *M* (Rast), 306. $C_{15}H_{10}N_4O_6,\frac{1}{2}H_2O$ requires C, 51·3; H, 3·2; N, 15·9%; *M*, 351].

3-*Cyano*-2,4,6-*triphenylcyclohex*-2-*en*-1-*ol*.—Potassium borohydride (0·8 g.) in water (5 c.c.) was added to 3-cyano-2,4,6-triphenylcyclohex-2-en-1-one (1·3 g.) in methanol (50 c.c.). After 5 hr. at room temperature the solution was poured into water, and the solid collected. The

required *cyclohexenol* (0·7 g.), needles, m. p. 124°, crystallised from ethyl acetate–light petroleum (Found: C, 85·0; H, 6·0; N, 4·4. $C_{25}H_{21}NO$ requires C, 85·4; H, 6·0; N, 4·0%).

Reaction of 3-Methoxy-5-phenylcyclohex-2-en-1-one with Acetone Cyanohydrin.—The enol ether (4·0 g.) was treated with acetone cyanohydrin (60 c.c.) containing methanolic potassium hydroxide as described in procedure (*a*). The resultant aqueous mixture was extracted with ethyl acetate. Distillation of the dried extract afforded a fraction, b. p. 160—162°/1·0 mm. (2·7 g.), consisting of unchanged enol ether and a substance which crystallised in the condenser. The latter was purified by resublimation *in vacuo*, followed by recrystallisation from light petroleum, to yield 2,2,5,5-tetramethyl-4-oxazolidone (0·3 g.), needles, m. p. 163° (Found: C, 58·2; H, 8·9; N, 10·2. Calc. for $C_7H_{13}NO_2$: C, 58·7; H, 9·1; N, 9·8%). Admixture with authentic material, m. p. 167°, prepared as described by Snyder and Elston,[7] did not depress the m. p.

3-Chloro-2-phenylcyclohex-2-en-1-one (V).—2-Phenylcyclohexane-1,3-dione (2·4 g.) in dry chloroform (10 c.c.) was refluxed with phosphorus trichloride (1·0 c.c.) for 3 hr. Crushed ice, ether, and aqueous sodium hydrogen carbonate were successively added, and the organic layer was separated, washed with 2N-sodium hydroxide, dried ($MgSO_4$), and evaporated. *3-Chloro-2-phenylcyclohex-2-en-1-one* (1·8 g.) crystallised from light petroleum as needles, m. p. 92° (Found: C, 69·3; H, 4·9; Cl, 17·5. $C_{12}H_{11}ClO$ requires C, 69·7; H, 5·4; Cl, 17·2%). This chloroketone (4·7 g.) was refluxed with potassium (0·7 g.) in dry t-butyl alcohol (80 c.c.) for 3·5 hr., then poured into water and extracted with ether. Concentration of the extract furnished a *substance* $C_{24}H_{20}O_2$, prisms, m. p. 206°, from ethyl acetate [Found: C, 84·4; H, 6·3; *M* (Rast), 353. $C_{24}H_{20}O_2$ requires C, 84·7; H, 5·9%; *M*, 340], which gave an *oxime sesquihydrate*, needles, m. p. 260°, from ethyl acetate (Found: C, 75·6; H, 6·1; N, 3·4. $C_{24}H_{21}NO_2,1{\cdot}5H_2O$ requires C, 75·4; H, 6·3; N, 3·7%).

4-Pyridylmethyl Cyanide.—4-Chloromethylpyridinium chloride (45·0 g.) [13] and potassium cyanide (45·0 g.) in methanol (400 c.c.) and water (200 c.c.) were refluxed for 2 hr. The solution was then concentrated, diluted with water, and extracted with ether. Distillation of the extract afforded a single fraction, b. p. 115—119°/3·5 mm., which crystallised when set aside for 1 hr. Redistillation furnished *4-pyridylmethyl cyanide* (13·0 g.), b. p. 92°/0·5 mm., m. p. 36° (Found: C, 69·4; H, 5·1; N, 22·7. $C_7H_6N_2$ requires C, 71·2; H, 5·1; N, 23·7%). This nitrile decomposed within a few days. Treatment with dry hydrogen chloride furnished the *hydrochloride*, needles, m. p. 270—272° (decomp.), from ethanol (Found: C, 54·5; H, 4·9; N, 17·7; Cl, 23·0. $C_7H_6N_2,HCl$ requires C, 54·4; H, 4·6; N, 18·1; Cl, 22·9%).

Ethyl 6-Cyano-5-oxo-6-4′-pyridylhexanoate (X).—4-Pyridylmethyl cyanide (14·7 g.) and diethyl glutarate (35·2 g.) were successively added to a solution of sodium (3·7 g.) in dry ethanol (80 c.c.), and the mixture was refluxed for 2 hr., set aside overnight, then concentrated, diluted with water, and washed with ether. Acidification of the aqueous fraction yielded *ethyl 6-cyano-5-oxo-6-4′-pyridylhexanoate* (19%), which recrystallised from benzene as prisms, m. p. 142° (Found: C, 64·7; H, 6·3; N, 10·6. $C_{14}H_{16}N_2O_3$ requires C, 64·6; H, 6·2; N, 10·8%).

Reaction of 2-Phenylcyclohexanone with Phosphorus Pentachloride.—The ketone (6·0 g.) was refluxed with phosphorus pentachloride (7·0 g.) in dry benzene (30 c.c.) for 2 hr. The resulting solution was poured on ice, neutralised with sodium hydrogen carbonate, and extracted with ether. Distillation of this extract gave a fraction, b. p. 132—138°/1·0 mm., which crystallised from light petroleum to give 2-phenylcyclohex-2-en-1-one (2·4 g.), needles, m. p. 94—95° (Found: C, 83·3; H, 6·8. Calc. for $C_{12}H_{12}O$: C, 83·7; H, 7·0%), undepressed on admixture with an authentic sample kindly supplied by Prof. D. Ginsberg.

2-Methoxy-1-phenylcyclohexan-1-ol.—2-Methoxycyclohexanone (1·9 g.) [14] in dry ether (10 c.c.) was added to phenylmagnesium bromide (from 2·4 g. of bromobenzene and 0·4 g. of magnesium) in dry ether and the mixture was refluxed for 1 hr. The complex was decomposed with ammonium chloride solution and extracted with ether. Distillation of the extract gave *2-methoxy-1-phenylcyclohexan-1-ol* (1·6 g.), b. p. 95—97°/0·5 mm., n_D^{20} 1·5370 (Found: C, 76·1; H, 8·8. $C_{13}H_{18}O_2$ requires C, 75·6; H, 8·8%). This alcohol was unchanged by treatment with benzoyl chloride in dry pyridine. The alcohol (3·0 g.) and phosphorus pentoxide (5·0 g.) in dry benzene (30 c.c.) were refluxed for 1 hr. The solution was filtered and distilled to give 2-phenylcyclohexanone (1·2 g.), m. p. and mixed m. p. 58° (from light petroleum).

Ultraviolet Spectra.—The ultraviolet absorption spectra of most of the compounds described are given in Table 3, for 96% ethanolic solutions, determined with a Unicam S.P. 500 Spectrophotometer. Italicised wavelengths denote an inflexion.

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TABLE 3

Compound	$\lambda_{max.}$ (mμ)	ε	Compound	$\lambda_{max.}$ (mμ)	ε	Compound	$\lambda_{max.}$ (mμ)	ε
(a) *Dienes*								
(IVa)	*229*	4,450	(If)	255	18,850	(IIb)	*231*	8,800
	279	9,800	(Ih)	265	14,100		282	12,900
(Id)	239	15,550		298	3,800	(XVIb)	260	10,700
	274	10,050	(XIIa)	264	15,700		271	12,100
						(XVId)	269	14,350
(b) *Derived enol ethers*								
(IVb)	232	8,900	(IIIc)	237	11,350	(XIV)	248	15,450
	269	13,850		280	10,750		*258*	14,950
(IVc)	232	9,300	(IIId)	256	23,000		*268*	13,750
	271	14,000	(IIIe)	268	16,050	(XVIc)	229	10,700
(IVd)	231	8,650	(XIIb)	258	15,200		*243*	8,300
	271	13,800	(IIc)	230	11,800		274	12,400
				273	14,200	(XVIe)	259	21,400
(c) *Exchange reaction products*								
(VIa)	235	10,550	(VIIb)	241	21,700	(VId)	*216*	21,800
	292	4,300		*247*	20,900		*237*	12,600
(VIb)	232	19,450	(XIII)	234	14,300		296	6,400
	335	4,000		*240*	13,950	(XV)	*224*	13,200
							292	7,600

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652. *Cyclohexane-1,3-diones. Part VII.*[1] *Reaction of 3-Methoxy-2,4-diphenylcyclohex-2-en-1-one with Acetone Cyanohydrin.*

By B. E. BETTS and W. DAVEY.

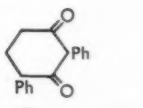
The study of the displacement of an alkoxyl group by a cyano-group by use of acetone cyanohydrin has now been extended to the enol ethers of unsymmetrically substituted cyclohexane-1,3-diones. 3-Cyano-2,4- and 3-cyano-2,6-diphenylcyclohex-2-enone were both obtained from 2,4-diphenylcyclohexane-1,3-dione and their structures were elucidated. Dehydrogenation of these cyano-ketones and related compounds afforded several new *m*-terphenyls substituted in the central ring.

IN previous parts[1,2] it has been shown that the enol ethers of 2-arylcycloalkane-1,3-diones react with acetone cyanohydrin to give the corresponding β-cyano-ketone. An unsymmetrically substituted compound such as 2,4-diphenylcyclohexane-1,3-dione (I), capable of giving rise to two enol ethers (IIa) and (IIb), should afford two corresponding cyano-ketones (IIIa) and (IIIb). It was hoped that the study of these compounds would afford more information about the exchange reaction.

2,4-Diphenylcyclohexane-1,3-dione (I) was prepared[3] by Robinson's modification of the Michael reaction. No crystalline enol ether was then isolated from treatment of this dione (I) with diazomethane, but reduction of the presumed mixture of isomers with lithium aluminium hydride gave, on dehydrogenation with sulphur, some 2'-hydroxy-*m*-terphenyl (Va). The action of diazomethane on the dione was re-investigated; the oil obtained gave a single enol ether, m. p. 137—138°, in 80% yield. The structure of this enol ether (IIa) or (IIb) was shown by reduction to the corresponding cyclohexenone, (IVa) or (IVb), which on dehydrogenation with sulphur gave 2'-hydroxy-*m*-terphenyl

[1] Part VI, preceding paper.
[2] Betts and Davey, Part V, *J.*, 1960, 1683.
[3] Ames and Davey, *J.*, 1958, 1794.

(Va).[4] This must have resulted from dehydrogenation of 2,6-diphenylcyclohex-2-en-1-one (IVa). In view of the accepted mechanism [5] of the lithium aluminium hydride reduction of the enol ethers of cyclohexane-1,3-diones, the enol ether, m. p. 137—138°, must be 3-methoxy-2,4-diphenylcyclohex-2-en-1-one (IIa).



(I)

(Va); R = Ph, R^1 = H, R^2 = OH

(Vb); R = H, R^1 = Ph, R^2 = OH

(VIII); R = Ph, R^1 = H, R^2 = CN

(IIa); R = Ph, R^1 = H, R^2 = OMe

(IIb); R = H, R^1 = Ph, R^2 = OMe

(IIIa); R = Ph, R^1 = H, R^2 = CN

(IIIb); R = H, R^1 = Ph, R^2 = CN

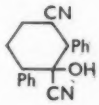
(IVa); R = R^2 = H, R^1 = Ph

(IVb); R = Ph, R^1 = R^2 = H

(VI); R = H, R^1 = Ph, R^2 = Cl

(VIIa); R = Ph, R^1 = H

(VIIb); R = H, R^1 = Ph



(IX)

(X)

Treatment of the dione (I) with phosphorus trichloride afforded the chloro-compound (VI) which was hydrogenated to 2,6-diphenylcyclohexanone (VIIa), whose structure was proved by the non-identity of its oxime with that of the alternative isomer (VIIb).[3] Selenium dehydrogenation of 2,6-diphenylcyclohexanone (VIIa) gave 2′-hydroxy-*m*-terphenyl (Va), whilst reaction with acetone cyanohydrin gave the corresponding cyanohydrin, which was acetylated and dehydrogenated to 2′-cyano-*m*-terphenyl (VIII).

Before examining the reaction of acetone cyanohydrin with the enol ether (IIa), we studied its reaction with the cyclohexenone (IVa); a di-adduct (IX), was the main product, and some mono-adduct (X) was also produced. The structures given were assigned on the basis of absorption spectra. There was no evidence to suggest that the di-adduct was a lactam (cf. Part V [2]).

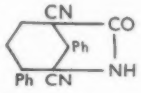
The exchange of acetone cyanohydrin with 3-methoxy-2,4-diphenylcyclohex-2-en-1-one (IIa) was studied at room temperature with triethylamine as catalyst; two isomers (IIIa and IIIb) (analysis and infrared spectra), m. p.s 121° and 158°, were obtained in 33% and 27% yield, respectively. With methanolic potassium hydroxide as catalyst the yields were 27% and 24%. Differentiation between these two isomers was achieved by consideration of the methylene absorptions in the spectra of chloroform solutions. The bands at 1451 cm.$^{-1}$ (IIIa) and 1450 cm.$^{-1}$ (IIIb) are ascribed to the methylene group adjacent to the phenyl group and the additional bands at 1417 cm.$^{-1}$ (isomer, m. p. 158°) and 1429 cm.$^{-1}$ (isomer, m. p. 121°) to the systems CH_2·CO and CH_2·C=C respectively.[6a] The isomer of m. p. 121° is therefore 3-cyano-2,4-diphenyl- (IIIa) and that of m. p. 158°, 3-cyano-2,6-diphenyl-cyclohex-2-en-1-one (IIIb). Proof was afforded by the observation that 3-cyano-2,5-diphenylcyclohex-2-en-1-one was converted by sodium hydroxide into 2′-hydroxy-*p*-terphenyl.[2] 3-Cyano-2,6-diphenylcyclohex-2-en-1-one (IIIb) reacted with sodium hydroxide to give 2′-hydroxy-*m*-terphenyl (Va); similarly, the isomer (IIIa) gave the isomeric 4′-hydroxy-*m*-terphenyl (Vb), m. p. 89°.[4] Since both these isomeric cyanoketones were obtained from a single enol ether (IIa) it appears that there is no single mechanism for the exchange and that cyanide attack can occur not only at the carbon atom to which the alkoxyl group is attached, but also at the carbonyl group.

Reaction of the cyano-compound (IIIb) with more acetone cyanohydrin at 90° furnished

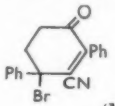
[4] Lüttringhaus and Saaf, *Annalen*, 1939, **542**, 241; 1945, **557**, 25.
[5] Frank and Hall, *J. Amer. Chem. Soc.*, 1950, **72**, 1645; Blanchard and Goering, *ibid.*, 1951, **73**, 5863; Born, Pappo, and Szmuskovicz, *J.*, 1953, 1779.
[6] Bellamy, "Infrared Spectra of Complex Molecules," Methuen, London, 1958, (*a*) p. **23**, (*b*) p. **139**.

XUM

a compound considered from its infrared spectrum and by analogy (Part V [2]) to be 1,5-dicyano-2,8-diphenyl-7-azabicyclo[3,2,1]octan-6-one (XI). When the cyano-compound (IIIa) was similarly treated, no crystalline product could be isolated.



(XI)



(XII)

(XIIIa); R = Ph, R¹ = H
(XIIIb); R = H, R¹ = Ph

Reduction of 3-cyano-2,4-diphenylcyclohex-2-en-1-one (IIIa) with potassium borohydride and bromination of the product gave a monobromo-derivative (XII) of the original cyano-ketone (IIIa), the frequency of the carbonyl absorption band (1686 cm.$^{-1}$) suggesting that the expected allylic bromination had occurred.[6b] This bromo-compound was dehydrobrominated to 2′-cyano-4′-hydroxy-*m*-terphenyl (XIIIa). Similar treatments of the isomeric 3-cyano-2,6-diphenylcyclohex-2-en-1-one (IIIb) yielded 4′-cyano-2′-hydroxy-*m*-terphenyl (XIIIb).

Experimental

" Light petroleum " refers to the fraction, b. p. 60—80°.

3-*Methoxy*-2,4-*diphenylcyclohex*-2-*en*-1-*one* (IIa).—2,4-Diphenylcyclohexane-1,3-dione (10·0 g.) (prisms, m. p. 180°, from methanol [3]) in methanol (20 c.c.) was treated with a slight excess of ethereal diazomethane. The product was distilled and a single fraction, b. p. 210—212°/1·0 mm., was collected and triturated with ether to yield 3-*methoxy*-2,4-*diphenylcyclohex*-2-*en*-1-*one* (80%), prisms, m. p. 137—138°, from light petroleum (Found: C, 81·6; H, 6·4. $C_{19}H_{18}O_2$ requires C, 81·2; H, 6·8%). This enol ether formed an *oxime*, prisms, m. p. 212°, from methanol (Found: C, 77·8; H, 6·5; N, 4·8. $C_{19}H_{19}NO_2$ requires C, 77·6; H, 6·5; N, 4·8%).

2,6-*Diphenylcyclohex*-2-*en*-1-*one* (IVa).—The preceding enol ether (10·0 g.) in dry ether (250 c.c.) was slowly added to a 2·8% ethereal solution of lithium aluminium hydride (50 c.c.), the mixture being cooled in ice–water. The solution was then refluxed for 1·5 hr. and decomposed with saturated ammonium chloride solution. The organic layer was extracted with ether and gave 2,6-*diphenylcyclohex*-2-*en*-1-*one* (8·0 g.), b. p. 167—168°/0·5 mm., n_D^{20} 1·6190 (Found: C, 86·8; H, 6·8. $C_{18}H_{16}O$ requires C, 87·1; H, 6·5%). Treatment of this ketone with hydroxylamine yielded 3-*hydroxyamino*-2,6-*diphenylcyclohexanone oxime*, needles, m. p. 196—197°, from ethanol (Found: C, 72·9; H, 7·0; N, 9·3. $C_{18}H_{20}N_2O_2$ requires C, 73·0; H, 6·8; N, 9·4%).

2,6-Diphenylcyclohex-2-en-1-one (2·0 g.) was heated with sulphur (0·3 g.) at 200—250° for 4 hr. to furnish 2′-hydroxy-*m*-terphenyl (0·5 g.), needles, m. p. and mixed m. p. 101°, from light petroleum.

3-*Chloro*-2,6-*diphenylcyclohex*-2-*en*-1-*one* (VI).—2,4-Diphenylcyclohexane-1,3-dione (10·0 g.) in dry chloroform (40 c.c.) was refluxed with phosphorus trichloride (2·9 g.) for 2·5 hr. Crushed ice, ether, and aqueous sodium hydrogen carbonate were successively added and the organic layer was separated, washed with aqueous sodium hydroxide, dried ($MgSO_4$), and evaporated. The residue was recrystallised from light petroleum and yielded the *chloro-compound* (6·7 g.), plates, m. p. 81° (Found: C, 76·8; H, 5·6; Cl, 13·2. $C_{18}H_{15}ClO$ requires C, 76·5; H, 5·3; Cl, 12·5%).

2,6-*Diphenylcyclohexanone* (VIIa).—The foregoing chloro-ketone (5·0 g.) in ethanol (120 c.c.) was shaken under hydrogen with palladous chloride (0·1 g.) and triethylamine (10 c.c.) until the theoretical volume of hydrogen had been absorbed. The solution was filtered, the solvent evaporated, and the residue washed with water and extracted with ether. Concentration of this extract gave 2,6-*diphenylcyclohexanone* (4·2 g.) which crystallised from light petroleum in needles, m. p. 124° (Found: C, 86·0; H, 7·1. $C_{18}H_{18}O$ requires C, 86·1; H, 7·1%) [*oxime*, needles, m. p. 175°, from ethyl acetate–light petroleum (Found: C, 81·2; H, 7·3; N, 5·6. $C_{18}H_{19}NO$ requires C, 81·5; H, 7·2; N, 5·3%)]. 4,6-Diphenylcyclohexanone oxime [3] has m. p. 212°. A mixture of the two oximes melted at 150—160°.

2′-*Hydroxy*-m-*terphenyl* (Va). The ketone (1·0 g.) mixed with selenium (1·0 g.) was heated at 300—350° for 6 hr., and the residue was extracted with light petroleum. 2′-Hydroxy-*m*-terphenyl (0·6 g.) crystallised from light petroleum in needles, m. p. 101° (Found: C, 87·6;

H, 5·8. Calc. for $C_{18}H_{14}O$: C, 87·8; H, 5·7%). Lüttringhaus and Saaf [4] record m. p. 101° for this isomer and m. p. 89° for the 4′-hydroxy-isomer.

1-Cyano-2,6-diphenylcyclohexan-1-ol.—13% Methanolic potassium hydroxide (0·1 c.c.) was added to 2,6-diphenylcyclohexanone (1·0 g.) in acetone cyanohydrin (10 c.c.), and the mixture was set aside overnight and then poured into water. The solid was filtered off, dried, and crystallised from ethyl acetate–light petroleum to yield the *cyano-derivative* (0·8 g.), needles, m. p. 183° (Found: C, 82·4; H, 6·8; N, 5·3. $C_{19}H_{19}NO$ requires C, 82·3; H, 6·9; N, 5·7%).

2′-Cyano-m-terphenyl (VIII).—1-Cyano-2,6-diphenylcyclohexan-1-ol (1·0 g.) was refluxed for 1 hr. with acetic anhydride (10 c.c.) containing one drop of concentrated sulphuric acid. The solution was poured into water (300 c.c.) and left overnight. The crude acetyl derivative thus obtained was heated at 350° for 3 hr. with selenium (1·0 g.). *2′-Cyano-m-terphenyl* (0·4 g.) crystallised from ethanol as needles, m. p. 135° (Found: C, 88·9; H, 5·0; N, 5·4. $C_{19}H_{13}N$ requires C, 89·4; H, 5·1; N, 5·5%).

Acetone Cyanohydrin Exchange Reactions.—(i) *With 2,6-diphenylcyclohex-2-en-1-one.* To 2,6-diphenylcyclohex-2-en-1-one (4·4 g.) in acetone cyanohydrin (10 c.c.) was added triethylamine (0·05 c.c.) and the mixture was set aside overnight. The solution was poured into water, and the product (1·8 g.) filtered off. Fractional crystallisation from methanol gave *1,3-dicyano-2,6-diphenylcyclohexan-1-ol* (1·1 g.), prisms, m. p. 228—229° (Found: C, 79·6; H, 6·2; N, 8·9. $C_{20}H_{18}N_2O$ requires C, 79·4; H, 6·0; N, 9·3%), $\nu_{max.}$ (KBr disc), 3411 (OH), 2247, and 2237 cm.$^{-1}$ (C⋮N); followed by *3-cyano-2,6-diphenylcyclohexan-1-one* (0·2 g.), needles, m. p. 208—209°, from ethyl acetate–light petroleum (Found: C, 82·5; H, 6·1; N, 5·1. $C_{19}H_{17}NO$ requires C, 82·9; H, 6·2; N, 5·1%), $\nu_{max.}$ (KBr disc) at 2237 (C⋮N) and 1718 cm.$^{-1}$ (C=O).

Treatment of 1,3-dicyano-2,6-diphenylcyclohexan-1-ol (0·3 g.) with acetic anhydride (5 c.c.) containing one drop of concentrated sulphuric acid gave the corresponding *acetate*, as plates, m. p. 211—212°, from ethyl acetate (Found: C, 77·0; H, 5·6; N, 8·1. $C_{22}H_{20}N_2O_2$ requires C, 76·7; H, 5·8; N, 8·1%).

(ii) *With 3-methoxy-2,4-diphenylcyclohex-2-en-1-one.* To the enol ether (1·0 g.) in acetone cyanohydrin (10 c.c.) was added triethylamine (0·05 c.c.). The mixture was set aside overnight and then poured into water and acidified (Congo Red). The aqueous solution was decanted, and the residual gum dissolved in hot methanol and left overnight. The solid was crystallised from ethyl acetate–light petroleum, furnishing *3-cyano-2,6-diphenylcyclohex-2-en-1-one* (0·26 g., 27%), prisms, m. p. 158—159° (Found: C, 83·1; H, 5·8; N, 5·1. $C_{19}H_{15}NO$ requires C, 83·5; H, 5·5; N, 5·1%). The infrared spectrum (Nujol mull) showed bands at 2215 (conjugated C⋮N), 1677 (αβ-unsaturated ketone), and 1581 cm.$^{-1}$ (phenyl system). Unchanged material was recovered from attempts to prepare an oxime. After the methanolic mother-liquor had been set aside for several days a second crop of crystals was collected and recrystallised from ethyl acetate–light petroleum, yielding *3-cyano-2,4-diphenylcyclohex-2-en-1-one* (0·32 g., 33%), needles, m. p. 121° (Found: C, 83·3; H, 5·8; N, 5·1%). The infrared spectrum (Nujol mull) showed bands at 2215 (conjugated C⋮N), 1677 (αβ-unsaturated ketone), 1599, and 1487 cm.$^{-1}$ (phenyl system). Treatment of this cyano-ketone with hydroxylamine afforded an *oxime*, needles, m. p. 237—238°, from ethanol (Found: C, 78·8; H, 5·7; N, 9·5. $C_{19}H_{16}N_2O$ requires C, 79·1; H, 5·6; N, 9·7%). When the exchange reaction was repeated with use of 13% methanolic potassium hydroxide (0·1 c.c.) as catalyst, a mixture of the two foregoing cyano-ketones (24% and 27%, respectively) was again isolated.

Action of Alkali on the Cyano-ketones.—3-Cyano-2,6-diphenylcyclohex-2-en-1-one (1·5 g.) in ethanol (70 c.c.) was refluxed with 20% aqueous sodium hydroxide (2 c.c.) for 2·5 hr. The solvent was evaporated under reduced pressure, the residue diluted with water, and the solid filtered off, dried, and extracted with light petroleum. 2′-Hydroxy-*m*-terphenyl (0·3 g.) crystallised from light petroleum as needles, m. p. and mixed m. p. 101°. This experiment was repeated with 3-cyano-2,4-diphenylcyclohex-2-en-1-one (1·5 g.), and the product was recrystallised from light petroleum, giving 4′-hydroxy-*m*-terphenyl (0·4 g.) as needles, m. p. 88·5° (Found: C, 88·2; H, 5·5. Calc. for $C_{18}H_{14}O$: C, 87·8; H, 5·7%). Lüttringhaus and Saaf [4] give m. p. 89°.

1,5-Dicyano-2,8-diphenyl-7-azabicyclo[3,2,1]*octan-6-one* (XI).—3-Cyano-2,6-diphenylcyclohex-2-en-1-one (1·0 g.) in acetone cyanohydrin (10 c.c.) containing triethylamine (0·05 c.c.) was refluxed for 45 min. The solution was poured into water, and the solid collected and dried. Recrystallisation from ethyl acetate furnished the *azabicyclo-ketone* (0·2 g., 19%), prisms, 220—222° (Found: C, 76·9; H, 5·3; N, 13·2. $C_{21}H_{19}N_3O$ requires C, 76·9; H, 5·2; N, 12·8%).

XUM

The infrared spectrum (KBr disc) showed bands at 3289 (NH, fused-ring γ-lactam), 2247 (C⋮N), 1715 (C=O; fused-ring γ-lactam), and 742 and 704 cm.$^{-1}$ (phenyl system). After several days the mother-liquor deposited unchanged cyano-ketone (0·4 g., 40%), m. p. and mixed m. p. 158°.

4-Bromo-3-cyano-2,4-diphenylcyclohex-2-en-1-one (XII).—3-Cyano-2,4-diphenylcyclohex-2-en-1-one (6·0 g.) in methanol (200 c.c.) was added to potassium borohydride (3·6 g.) in water (30 c.c.), and the mixture set aside for 5 hr. The solution was poured into water, and the semi-solid collected. All attempts to crystallise this material were unsuccessful. To this oil in dry carbon tetrachloride (100 c.c.) was added *N*-bromosuccinimide (4·2 g.) and benzoyl peroxide (0·05 g.), and the mixture was refluxed for 2 hr. The succinimide was filtered off, and the carbon tetrachloride evaporated under reduced pressure. The residual gum was triturated with benzene to yield *4-bromo-3-cyano-2,4-diphenylcyclohex-2-en-1-one* (1·2 g.), prisms, m. p. 149°, from ethyl acetate (Found: C, 64·9; H, 4·3; N, 4·0; Br, 22·6. $C_{19}H_{14}BrNO$ requires C, 64·7; H, 4·0; N, 4·0; Br, 22·7%). The infrared spectrum (KBr disc) showed bands at 2208 (conjugated C⋮N), 1686 (αβ-unsaturated ketone), and 544 cm.$^{-1}$ (C–Br).

2′-Cyano-4′-hydroxy-m-terphenyl (XIIIa).—The foregoing bromo-compound (1·0 g.) in dry pyridine (10 c.c.) was refluxed for 1 hr., the solution poured into dilute hydrochloric acid, and the product filtered off. *2′-Cyano-4′-hydroxy-m-terphenyl* crystallised from ethyl acetate–light petroleum as needles, m. p. 183° (Found: C, 83·9; H, 4·7; N, 5·2. $C_{19}H_{13}NO$ requires C, 84·1; H, 4·7; N, 5·2%).

3-Cyano-2,6-diphenylcyclohex-2-en-1-ol.—3-Cyano-2,6-diphenylcyclohex-2-en-1-one (1·6 g.) in methanol (60 c.c.) was added to potassium borohydride (1·0 g.) in water (10 c.c.). After 5 hr. the solution was poured into water, and the precipitate (1·6 g.) collected and dried. *3-Cyano-2,6-diphenylcyclohex-2-en-1-ol* (0·8 g.) crystallised from benzene–light petroleum as prisms, m. p. 113—114° (Found: C, 83·2; H, 6·3; N, 5·2. $C_{19}H_{17}NO$ requires C, 82·9; H, 6·2; N, 5·1%).

4′-Cyano-2′-hydroxy-m-terphenyl (XIIIb).—*N*-Bromosuccinimide (3·5 g.) and benzoyl peroxide (0·05 g.) were refluxed with 3-cyano-2,6-diphenylcyclohex-2-en-1-ol (5·0 g.) in dry carbon tetrachloride (150 c.c.) for 2 hr. The succinimide was filtered off, and the filtrate concentrated. The resulting uncrystallisable oil was refluxed for 1 hr. in dry pyridine (10 c.c.), and the solution poured into dilute hydrochloric acid. The solid was collected and crystallised from ethyl acetate to yield *4′-cyano-2′-hydroxy-m-terphenyl* (0·7 g.), prisms, m. p. 146° (Found: C, 84·5; H, 4·8; N, 5·6. $C_{19}H_{13}NO$ requires C, 84·1; H, 4·7; N, 5·2%).

2,4,5-Triphenylcyclohexane-1,3-dione.—To sodium (1·6 g.) in dry ethanol (100 c.c.) was added ethyl phenylacetate (8·2 g.) followed by 1,4-diphenylbut-3-en-2-one (11·1 g.), and the mixture was refluxed for 3 hr. and then set aside overnight. The solvent was evaporated, the residue diluted with water, and the remaining solid was filtered off. *Acidification of the filtrate afforded 2,4,5-triphenylcyclohexane-1,3-dione* (2·7 g.), needles, m. p. 204°, from methanol (Found: C, 85·2; H, 5·7. $C_{24}H_{20}O_2$ requires C, 84·7; H, 5·9%). Use of ethyl phenylmalonate (11·8 g.) in place of ethyl phenylacetate likewise furnished the dione (0·6 g.), m. p. and mixed m. p. 204°.

3-Methoxy-2,4,5(or 2,5,6)-triphenylcyclohex-2-en-1-one.—Treatment of the dione (1·3 g.) in methanol with a slight excess of ethereal diazomethane gave a single *enol ether* (0·5 g.), prisms,

Compound	$\lambda_{max.}$ (mμ)	ε	Compound	$\lambda_{max.}$ (mμ)	ε	Compound	$\lambda_{max.}$ (mμ)	ε	Compound	$\lambda_{max.}$ (mμ)	ε
				(a) Products from reactions with acetone cyanohydrin							
IIIa	236	11,400	XI	*335*	3650	IX	241	572	X	241	471
	297	5400		*257*	2000		246·5	587		247	514
IIIb	*234*	11,050		263·5	1800		251·5	687		251·5	613
	292	4200		*268*	1700		257	716		257·5	707
				291	1800		263	629		263·5	589
							267	429		267	405
				(b) Terphenyls							
Va *	238	25,100	VIII	*224*	23,500	XIIIa	225	33,950	XIIIb	*220*	27,950
	295	5100		242	22,700		*239*	24,500		266	13,850
Vb	247	27,300		300	4900		320	8350		312	8400
	268	16,800									
	302	4200									
				(c) Other compounds							
I	*232*	8600	IIa	231	9450	VI	*215*	14,500	XII	229	15,700
	270	12,700		271	12,850		*230*	11,300		306	5600
						IVa	*240*	8900			

* Ames and Davey [3] report $\lambda_{max.}$ 238 (ε 22,200) and 295 mμ (ε 4820) in ethanol.

m. p. 137—138°, from methanol (Found: C, 84·5; H, 6·5; OMe, 8·2. $C_{25}H_{22}O_2$ requires C, 84·7; H, 6·3; OMe, 8·8%).

Ultraviolet Spectra.—The absorption spectra, recorded in the Table were determined for 96% ethanolic solutions with a Unicam S.P. 500 spectrophotometer. Italicised values denote inflexions.

We thank Miss E. M. Tanner, Parke, Davis & Co., Hounslow, Middlesex, for determining some of the infrared spectra and for helpful suggestions on their interpretation.

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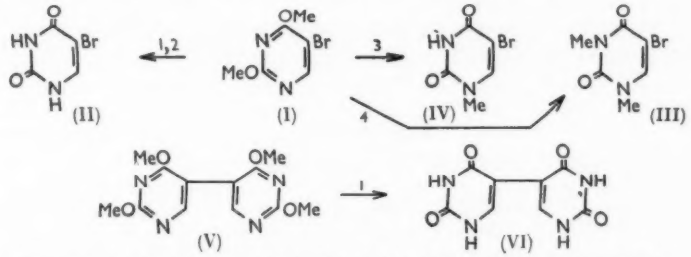
653. *Sodium Iodide in Acetic Acid as a Mild Dealkylating Agent.*

By T. L. V. ULBRICHT.

Hydrogen bromide in acetic acid is the best of the strongly acidic reagents for dealkylating alkoxypyrimidines. The much milder reagent, sodium iodide in acetic acid, was found to dealkylate alkoxypyrimidines in 80—100% yield. 2-Methoxypyridine also reacted readily, but *p*-nitroanisole was unaffected, and 2,4-dinitroanisole and 4-methoxypyridine *N*-oxide reacted to only a small extent. With sodium iodide in acetonylacetone, a 2,4-dimethoxypyrimidine rearranged to the corresponding 1,3-dimethyluracil.

IN connection with another problem, a method was required for dealkylating alkoxypyrimidines under relatively mild conditions. This reaction is usually accomplished with strong acids, for example, ethanolic hydrogen chloride [1] or concentrated hydrochloric acid.[2] In fact the most efficient reagent appears to be hydrogen bromide in glacial acetic acid; bromide is a stronger nucleophile than chloride ion, and acetic acid is an excellent solvent for alkoxypyrimidines, which are usually insoluble in water. 5-Bromo-2,4-dimethoxypyrimidine (I), available from other studies, was used as a test compound. It was converted into 5-bromouracil (II) by hydrogen bromide in acetic acid, in virtually quantitative yield in 2 hours at 70° and in 60% yield in 24 hours at room temperature (after being warmed for a few minutes at 50° to effect dissolution). Similarly, bi-(2,4-dimethoxypyrimidin-5-yl) [3] (V) was converted into biuracil-5-yl (VI).



Reagents: 1, HBr–AcOH. 2, NaI–AcOH. 3, NaI–AcOH–CH_2Ac_2. 4, NaI–CH_2Ac_2.

By using a more nucleophilic ion, it should be possible to effect the same reaction without resort to strong acid, and thus sodium iodide in acetic acid was tried. Conversion

[1] Hilbert and Johnson, *J. Amer. Chem. Soc.*, 1930, **52**, 4489.
[2] Ulbricht, *Tetrahedron*, 1959, **6**, 225.
[3] Ulbricht, unpublished work.

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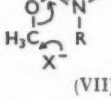
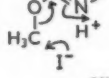
of the ether (I) into the uracil (II) by an excess of this reagent was 82% complete in 4 hours at 100° and 67% in 3 hours (all experiments were on a 500 mg. scale; working-up losses would be less, and the yields higher, on a larger scale). When exactly one molar equivalent of sodium iodide was used 40% of the uracil was obtained, together with unchanged ether; an intermediate was not isolated.

The mechanism of the reaction can be envisaged as involving two steps, protonation of nitrogen followed by attack by iodide ion (VII; R = H, X = I), as in the Hilbert–Johnson synthesis of glycosylpyrimidines [1] from alkoxypyrimidines and glycosyl halide RX; * alternatively, it might involve a concerted mechanism (VIII), analogous to the reaction of *O*,2′-cyclouridine with iodide ion in the presence of acetic acid [4] (cf. IX). In the latter case, no reaction takes place in the absence of acid; with the pyrimidine (I), a different reaction occurs with sodium iodide in a non-acidic solvent (see below).

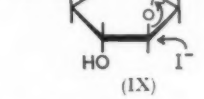
2-Methoxypyridine is readily converted into 2-pyridone by sodium iodide in acetic acid; but 4-methoxypyridine *N*-oxide, for the demethylation of which a strictly analogous mechanism cannot be written, was recovered unchanged, though some reaction must have occurred, since free iodine was liberated. No reaction took place with *p*-nitroanisole, and 2,4-dinitroanisole was demethylated only to the extent of 8% in 3 hours at 100°. The much greater activating effect of a ring-nitrogen atom than of two *op*-nitro-groups in a benzene ring is noteworthy, and is undoubtedly due to the fact that the nitro-compounds are much weaker bases.



(VII)



(VIII)



(IX)

With sodium iodide in acetonylacetone, the pyrimidine (I) undergoes $O \longrightarrow N$ alkyl rearrangement. As is to be expected, this reaction is slower than demethylation, and the yield of 5-bromo-1,3-dimethyluracil (III) was 35% after 3 hours at 100° and 75% after 6 hours. Hilbert and Johnson [1] found that alkyl iodides readily effected the rearrangement of the 2-alkoxy-group in such compounds; for example, 2,4-dimethoxypyrimidine gave 4-methoxy-1-methylpyrimid-2-one, but that heating to 220—240° was necessary to rearrange both groups.[6] It would be of interest to see whether sodium iodide (or lithium bromide) in a suitable solvent could be used to effect the rearrangement of *O*-glycosyl- to *N*-glycosyl-pyrimidines.

When the pyrimidine (I) was heated with sodium iodide in acetonylacetone containing 10% of acetic acid, 5-bromo-1-methyluracil (IV) was isolated.

Experimental

Light petroleum refers to the fraction of b. p. 60—80°.

Demethylations with Hydrogen Bromide.—(1) *5-Bromo-2,4-dimethoxypyrimidine* (I). (*a*) The pyrimidine [7] (I) (500 mg.) was refluxed for 30 min. in a 50% w/v solution of hydrogen bromide in glacial acetic acid (5 c.c.). Water (5 c.c.) was added, and the solution cooled to 0°. The yield of 5-bromouracil was 355 mg. (81%), and the m. p. and mixed m. p. (insertion at 290°)

* Ionisation of the glycosyl halide proceeds by neighbouring-group participation of the 2-acyloxy-group.[5]

[4] Brown, Parihar, and Sir Alexander Todd, *J.*, 1958, 4242.
[5] Baker, Joseph, Schaub, and Williams, *J. Org. Chem.*, 1954, **19**, 1786.
[6] Hilbert and Johnson, *J. Amer. Chem. Soc.*, 1930, **52**, 2001.
[7] Hilbert and Jansen, *J. Amer. Chem. Soc.*, 1934, **56**, 134.

310° (lit.,[7] m. p. 312°). (*b*) A similar experiment in which the reactants were left at room temperature for 24 hr., then heated at 50—60° for 1 hr. and 60—70° for 1 hr., and finally evaporated to dryness gave 402 mg. (92%) of the uracil. (*c*) In a third experiment the reactants were warmed, with shaking, at 50° until the pyrimidine dissolved (8 min.), then left for 24 hr. at room temperature. The yield was 260 mg. (60%).

(2) *Bi-(2,4-dimethoxypyrimidin-5-yl)* (V). The bipyrimidinyl[8] (150 mg.) was heated in 50% w/v hydrogen bromide–acetic acid (5 c.c.) on a steam-bath for 3 hr. The solvent was removed under reduced pressure, and the product warmed with water, cooled, filtered off, and washed with ethanol. The yield of *biuracil-5-yl* (VI) was 120 mg. (99%). Recrystallisation from water gave pale buff needles, no m. p. <300° (Found: C, 41·8; H, 2·9; N, 23·8. $C_8H_6N_4O_4,\frac{1}{2}H_2O$ requires C, 41·6; H, 3·0; N, 24·2%).

Demethylations with Sodium Iodide in Acetic Acid.—(1) *Pyrimidine* (I). (*a*) The pyrimidine (I) (500 mg.) was heated with sodium iodide (1·0 g.) in glacial acetic acid (5 c.c.) on a steam-bath for 4 hr. The solvent was removed under reduced pressure, and the residue washed with benzene, then boiled with water (5 c.c.) and a little sodium thiosulphate, to give a colourless solution, which was cooled to 0°. The yield of 5-bromouracil was 291 mg. (82%). After 3 hr. the yield was 67%. (*b*) Reaction as in (*a*), but with 342 mg. (1·0 mol.) of sodium iodide, gave a product that was washed with light petroleum, leaving 175 mg. (40%) of 5-bromouracil. From the filtrate, unchanged ether, m. p. and mixed m. p. 62—64°, was isolated.

(2) *2-Methoxypyridine.* 2-Methoxypyridine (100 mg.) and sodium iodide (250 mg.) were heated in glacial acetic acid (5 c.c.) on a steam-bath for 3 hr. The solvent was evaporated, ethanol and benzene were added, and the whole was evaporated. The residue was extracted with hot benzene, and the greenish solid obtained on evaporation of the extract was again extracted with benzene; this extract was concentrated, giving colourless 2-pyridone (correct infrared spectrum).

(3) *4-Methoxypyridine N-oxide.* The *N*-oxide (330 mg.) and sodium iodide (1·0 g.) were heated in glacial acetic acid (10 c.c.) on a steam-bath for 3 hr. The solvent was removed from the dark brown solution under reduced pressure, and sodium thiosulphate solution and chloroform were added. The residue obtained from the chloroform extract was recrystallised from benzene, giving the unchanged oxide, m. p. and mixed m. p. 81—82°.

(4) *p-Nitroanisole.* *p*-Nitroanisole (1·0 g.) and sodium iodide (2·0 g.) were heated in glacial acetic acid (10 c.c.) on a steam-bath for 3 hr. There was almost quantitative recovery of *p*-nitroanisole, m. p. and mixed m. p. 52—53°.

(5) *2,4-Dinitroanisole.* 2,4-Dinitroanisole (5 g.) and sodium iodide (10 g.) were heated in glacial acetic acid (50 c.c.) on a steam-bath for 3 hr. The solvent was removed under pressure, and ethyl acetate and dilute sodium hydroxide solution containing a little sodium thiosulphate were added to the residue. After being washed with ethyl acetate, the aqueous layer was acidified with hydrochloric acid, heated until the product dissolved, treated with charcoal, and filtered, giving, on cooling, 2,4-dinitrophenol (400 mg.), m. p. 111—113°, mixed m. p. 112—114°. The ethyl acetate layer gave 4·4 g. of unchanged dinitroanisole, m. p. 86° (from ethanol).

Rearrangement with Sodium Iodide in Acetonylacetone.—The pyrimidine (I) (500 mg.) was heated with sodium iodide (1·0 g.) in acetonylacetone (5 c.c.) on a steam-bath for 6 hr. The solvent was removed under reduced pressure, a little water added, and the product filtered off. After washing with light petroleum there remained 5-bromo-1,3-dimethyluracil (III) (375 mg., 75%), m. p. and mixed m. p. 184—185° (corr.) (from benzene) (lit.,[8] 181—182°). The yield after 3 hr. was 35%. No reaction took place in acetonylacetone without sodium iodide in 6 hr. at 100°.

Reaction with Sodium Iodide and Acetic Acid in Acetonylacetone.—The pyrimidine (I) (500 mg.) and sodium iodide (1·0 g.) were heated with acetic acid (0·5 c.c.) in acetonylacetone (5 c.c.) on a steam-bath for 6 hr. The solvent was removed under reduced pressure, and the residue extracted with light petroleum (discarded) and crystallised from water, to give a product (288 mg., 60%) of indefinite m. p. 200—230°. After several recrystallisations from aqueous ethanol it had m. p. 264—266° (Found: C, 29·7; H, 2·7; N, 13·9. Calc. for $C_5H_5BrN_2O_2$: C, 29·3; H, 2·5; N, 13·7%). Comparison with 5-bromo-1-methyluracil[9] showed that the compounds were identical (mixed m. p. 265—267°).

[8] Johnson and Clapp, *J. Biol. Chem.*, 1908, **5**, 49.
[9] Benitez, Ross, Goodman, and Baker, *J. Amer. Chem. Soc.*, 1960, **82**, 4585.

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The author thanks Professor Sir Alexander Todd for his interest, Dr. D. M. Brown for a discussion, and Dr. A. R. Katritzky for samples of 2-methoxypyridine and 4-methoxypyridine-*N*-oxide. This work was carried out during the tenure of an I.C.I. Fellowship.

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654. *The Reactions of Diboron Tetrachloride with Some Nitrogen-containing Donor Molecules.*

By A. K. HOLLIDAY, F. J. MARSDEN, and A. G. MASSEY.

The adducts $2D,B_2Cl_4$ are formed by direct reaction of diboron tetrachloride with D = Me_3N, C_5H_5N, MeCN, and HCN; these are involatile and thermally stable and do not react with olefins. Addition of hydrogen chloride can give diborates, *e.g.*, $[Me_3NH]_2[B_2Cl_6]$, and the methyl cyanide adduct adds trimethylamine with only partial displacement of the cyanide, suggesting formation of $[Me_4N]_2[B_2Cl_4(CN)_2]$. With D = $(CH_2{\cdot}NMe_2)_2$, a 1 : 1 adduct is formed which is polymeric; with D = N_2H_4, $NH_2{\cdot}NMe_2$, and $(CH_2{\cdot}NH_2)_2$, elimination of hydrogen chloride as the hydrochloride follows donation and polymeric B–N compounds containing boron–boron bonds are formed. D = Me_2NH gives a mixture of $B(NMe_2)_3$, $B_2(NMe_2)_4$, and polymeric $BNMe_2$.

PREVIOUS studies of the reactions of diboron tetrachloride with ammonia and amines [1] and with cyanogen [2] have shown that both boron atoms act as acceptors, giving 2 : 1 adducts. When the donor molecule contains reactive hydrogen, elimination of hydrogen chloride as the hydrochloride of the donor base follows, *e.g.*: [1]

$$B_2Cl_4 + 8Me_2NH \longrightarrow B_2(NMe_2)_4 + 4Me_2NH,HCl$$

We now report the reactions of diboron tetrachloride with both mono- and bi-dentate nitrogen-donor molecules.

EXPERIMENTAL

Diboron tetrachloride was prepared and purified as previously described.[3] Donor substances were prepared (where necessary) by conventional methods and purified by fractionation in the vacuum-system. In a typical reaction, measured amounts of diboron tetrachloride and the donor were mixed at liquid-nitrogen temperature and the mixture was allowed to warm until reaction was observed (usually at the m. p. of the donor); the reaction temperature was kept as low as possible to minimise decomposition of the unchanged diboron tetrachloride. Decomposition was, however, often catalysed by the donor, and hence precise reaction ratios could not always be observed. When reaction was complete, the excess of donor was removed and measured, together with any volatile products which were separated and identified. The reaction product was examined (*a*) by hydrolysis in a sealed tube (evolved hydrogen and chloride ion were determined, but accurate boron determinations were usually nullified by interference of the donor base in the titrations), (*b*) by heating it in a sealed tube, volatile products being removed as before, (*c*) by addition of ethylene or but-2-ene, and (*d*) by addition of hydrogen chloride or trimethylamine. The decomposition of diboron tetrachloride during reaction with a donor yielded boron trichloride and polymeric BCl, the latter being red or yellow; separate experiments indicated that the rate of reaction of $(BCl)_n$ with a donor was negligibly slow under the conditions used. Hence the main product was contaminated with small amounts of the donor–boron trichloride adduct and with $(BCl)_n$. Reaction of an excess

[1] Urry, Wartik, Moore, and Schlesinger, *J. Amer. Chem. Soc.*, 1954, **76**, 5293.
[2] Apple and Wartik, *J. Amer. Chem. Soc.*, 1958, **80**, 6158.
[3] Holliday and Massey, *J.*, 1960, 43.

of diboron tetrachloride with a donor appeared to yield the same product as when an excess of donor was used, the unchanged tetrachloride forming more trichloride and $(BCl)_n$; such reactions were not, therefore, studied in detail. The amount of reaction product in an experiment was usually 0·5—1·0 mmole.

Results and Discussion

The results are summarised in the Table. The quoted reaction ratios represent the mean of at least two (usually four) determinations, except that for hydrogen cyanide which is the value of a single observation. The donors listed in the top part of the Table each gave only a solid adduct with no other products; in the lower part, elimination of hydrogen chloride as the donor hydrochloride occurred.

Trimethylamine.—The adduct $2NMe_3,B_2Cl_4$ was formed readily as a white solid. In the previously reported preparation [1] a sublimate from the adduct was soluble in benzene and gave a cryoscopic molecular weight corresponding to $[(NMe_3)_2B_2Cl_4]_4$. Our specimen was almost insoluble in benzene (0·3%) and molecular-weight determinations were insufficiently precise to have meaning. Almost quantitative 2 : 1 addition of hydrogen chloride to the adduct occurred slowly, without evolution of any volatile product other than a trace of hydrogen; there was no evidence for the formation of diboron tetrachloride or its decomposition products. A similar addition of hydrogen chloride to the adducts

Donor (D)	Reaction ratio (D : B_2Cl_4)	Products	Thermal stability	Hydrolysis products (%) H_2	Hydrolysis products (%) Cl	Addition per mole of adduct HCl	Addition per mole of adduct NMe_2
Me_3N	1·92	Solid adduct	High	—	—	1·92	—
C_5H_5N	1·98	,,	,,	46	99·5	0·25	—
MeCN	1·95	,,	Decomp. <130°	90	98	—	1·95
HCN	1·92	,,	—	—	—	—	—
$(CH_2{\cdot}NMe_2)_2$	1·06	,,	High	82	98	0·55	—
N_2H_4	4·9	$(B_2N_2)_n$ + HCl	—	30—55	—	—	—
$NH_2{\cdot}NMe_2$....	3·05	$(BClNMe)_n$ + HCl	—	2—55	—	—	—
$(CH_2{\cdot}NH_2)_2$	5·07	$[B_2N_2(CH_2)_2]_n$ + HCl	—	90	—	—	—
Me_2NH	7·32	$B(NMe_2)_3$, $B_2(NMe_2)_4$, $(BNMe_2)_n$ + HCl	—	—	—	—	—

$2Me_3N,Cl_2B{\cdot}CHR{\cdot}CHR{\cdot}BCl_2$ (R = H or Me) has been attributed to formation of compounds $[Me_3NH]_2[Cl_3B{\cdot}CHR{\cdot}CHR{\cdot}BCl_3]$ [3,4] and formation of a hexachlorodiborate $[Me_3NH]_2[B_2Cl_6]$ is probable here; hydrolysis after addition of the hydrogen chloride indicated no loss of boron–boron bonding. Evidence for the formation of the $[B_2Cl_6]^{2-}$ ion has been obtained in the titration of diboron tetrachloride with tetramethylammonium chloride in anhydrous hydrogen chloride as solvent.[5] The trimethylamine–diboron tetrachloride adduct did not react with ethylene.

Pyridine.—The adduct $2py,B_2Cl_4$ was formed by a vigorous reaction which occurred when the mixture was warmed to the melting point of pyridine; a yellow coloration suggested formation of some $(BCl)_n$. Hydrolysis of the adduct gave a very low yield of hydrogen, either because B–B bonding had been lost by some intramolecular rearrangement or because reduction of the pyridine rings occurred on hydrolysis [formation of any py,BCl_3 requires formation of an equal amount of (BCl) which yields hydrogen on hydrolysis; hence the low hydrogen figure could not be due to decomposition of the tetrachloride]. When the adduct was heated to ~200°, there were no volatile products (other than a trace of pyridine probably occluded in the adduct) and no change in appearance, but the hydrogen yield on hydrolysis had fallen to 16%. Uptake of hydrogen chloride by the adduct was apparently incomplete even after 40 hours' heating at 100° and did not approach the 2 mol. expected for a pyridine adduct, where formation of a dipyridinium hexachlorodiborate might be expected. These observations suggest that

[4] Feeney, Holliday, and Marsden, *J.*, 1961, 356.
[5] Holliday, Peach, and Waddington, *Proc. Chem. Soc.*, 1961, 220.

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some rearrangement of the adduct occurs on formation and is taken further on heating; it is to be noted that the pyridine–boron trichloride adduct may well have a structure $[py_2BCl_2][BCl_4]$,[6] and some similar structure may obtain for the rearranged tetrachloride adduct. There was no reaction of the adduct with ethylene.

Methyl Cyanide and Hydrogen Cyanide.—Since addition to diboron tetrachloride can occur by π-donation,[7,8] there was the possibility of 1 : 1 addition of either of these donors through the C–N π-bond. The observed reaction ratio was 2 : 1 (even when excess of the tetrachloride was used), and only traces of other volatile products were formed; one of these was hydrogen chloride; the others were not identified. Reaction of hydrogen chloride with methyl cyanide to give 1,1-dichloroethylamine[9] did not occur under the conditions used in our experiments. There was less evidence of decomposition of the tetrachloride when the methyl cyanide adduct was formed than in other donor reactions. The adduct $2MeCN,B_2Cl_4$ was more rapidly hydrolysed than the trimethylamine or pyridine adducts, and the hydrogen recovery indicated that B–B bonding was retained. The adduct was also less stable thermally, and heating at 130° for some hours gave a sublimate of methyl cyanide–boron trichloride with small amounts of free methyl cyanide and a residue having the characteristic yellow colour of $(BCl)_n$. This result clearly suggests dissociation of the adduct on heating, the liberated cyanide then combining with the boron trichloride which would be formed rapidly from the tetrachloride at 130°. The stability of the tetrachloride adduct was sufficient to prevent reaction with ethylene, which did not occur even after many days at 20°. However, trimethylamine reacted readily at 20° and 2 mol. were taken up, suggesting complete displacement of the cyanide. Unexpectedly, the amount of methyl cyanide recovered was much less than 2 mol.—the average recovery from four experiments was 50%. Also, the remaining solid became orange-red in contact with the trimethylamine, and the same colour was observed if less than 2 mol. of trimethylamine were added to 1 mol. of the cyanide adduct. When methyl cyanide was added to the white trimethylamine adduct $2Me_3N,B_2Cl_4$, uptake of some cyanide and a colour change to orange-red occurred slowly on storage. Hydrolysis of the adduct $2MeCN,B_2Cl_4$ to which trimethylamine had been added gave a 75% recovery of hydrogen on hydrolysis, compared with 90% from the original adduct. The infrared spectrum of the red solid formed when trimethylamine was added showed absorption peaks similar to those observed for trimethylamine–diboron tetrachloride, together with some additional peaks which could not be assigned.

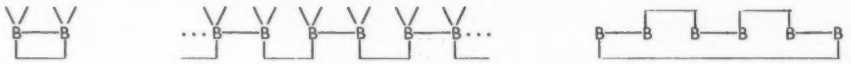
These observations suggest that displacement of methyl cyanide by trimethylamine occurs to a limited extent, but that fission of co-ordinated methyl cyanide also occurs to form a quaternary dicyanodiborate, analogous to the hexachlorodiborate:

$$2MeCN,B_2Cl_4 + 2Me_3N \longrightarrow [Me_4N]_2[(CN)BCl_2{\cdot}BCl_2(CN)]$$

Hydrogen cyanide formed a white solid $2HCN,B_2Cl_4$ similar to the methyl cyanide adduct. When hydrogen cyanide was kept in contact with the trimethylamine–diboron tetrachloride adduct for some hours, first at 20° and then at 100°, 1·8 mol. of hydrogen cyanide were taken up per mol. of adduct without evolution of trimethylamine or other volatile product, and again the solid became red, again suggesting formation of the compound $[Me_3NH]_2[B_2Cl_4(CN)_2]$. As further evidence, the white 1 : 1 adduct $MeCN,BCl_3$ was prepared by direct addition *in vacuo*,[10] and on addition of excess of trimethylamine 1 mol. was gradually taken up and only 5% of the theoretical amount of methyl cyanide liberated, the colour becoming orange-red. Here also the predominant reaction is the formation of a cyano-trichloroborate $[NMe_4][BCl_3(CN)]$, and the colour appears to be a property associated with anionic B–CN bonding and not with the B–B bond.

[6] Greenwood and Wade, *J.*, 1960, 1130.
[7] Holliday, Massey, and Taylor, *Proc. Chem. Soc.*, 1960, 359.
[8] Holliday and Massey, *J. Inorg. Nuclear Chem.*, 1961, **18**, 108.
[9] Hinkel and Treharne, *J.*, 1954, 866.
[10] Laubengayer and Sears, *J. Amer. Chem. Soc.*, 1945, **67**, 164.

NNN'N'-*Tetramethylethylenediamine.*—Reaction of a bidentate donor with diboron tetrachloride is of interest because co-ordination may occur with a single molecule (I) or by linking molecules (II) with the possibility of ring formation (III). A vigorous reaction



(I) (II) (III)

with the diamine (tmen) occurred at the melting point of the latter; it was difficult to remove all the unchanged diamine from the white solid product, but the reaction ratio was sufficiently close to 1 : 1 to indicate donation by both nitrogen atoms. A trace of volatile white solid too small for identification was removed with the unchanged amine, but the bulk of the product was involatile and insoluble in benzene, suggesting a structure of type (II) or (III) rather than (I). Hydrolysis gave slow but quantitative recovery of chloride and the hydrogen yield indicated that most of the B–B bonding was retained in the adduct. Reaction with hydrogen chloride was also slow, and after many hours at 20°, followed by heating, only about half a mol. per mol. of adduct was taken up. The only volatile product was a small amount of hydrogen, and there was no evidence of free diboron tetrachloride or its decomposition products. Hydrolysis yielded all the chlorine as chloride, and the hydrogen yield was 73%, only a small decrease compared with the original adduct. Reaction of an adduct of type (I) with hydrogen chloride to give $[tmenH_2][B_2Cl_6]$ seems feasible; reaction with a compound of type (II), which might be highly polymerised, could be less easy; moreover, attack on such a structure might be as likely at the B–B as at the B–N bonds, *i.e.*, the reaction

$$-NMe_2{\cdot}BCl_2{\cdot}BCl_2{\cdot}NMe_2- + 2HCl \longrightarrow 2(-NMe_2{\cdot}BCl_2) + H_2$$

could occur. The evidence is therefore again in favour of the structure (II), with some reaction to give a diborate but also slight attack on the B–B bonding to give hydrogen, with consequent loss of the latter on hydrolysis. An attempt to convert the original adduct into the boron trichloride adduct, by attacking the B–B bond with chlorine, was unsuccessful; only slight uptake of chlorine occurred, and the simultaneous liberation of hydrogen chloride indicated attack on the methylene groups rather than on the B–B bonds. No boron trichloride adduct could be identified in the product.

Hydrazine and NN-*Dimethylhydrazine.*—The reaction ratio 5 for addition of hydrazine indicated initial donation by both nitrogen atoms, followed by elimination of 4 mol. of hydrogen chloride as hydrazine hydrochloride, *i.e.*:

$$B_2Cl_4 + 5N_2H_4 \longrightarrow 4N_2H_5Cl + B_2N_2$$

With the dimethylhydrazine, elimination of only two mol. of hydrogen chloride could occur, giving the observed ratio 3 : 1; the reactions are generally similar to those observed by Nöth [11] between alkyl- and aryl-boron halides and hydrazines, in which, *e.g.*, a compound $R_{3-n}BCl_n$ reacted with $(n + \frac{1}{2})$ mol. of hydrazine with formation of the hydrochloride. With either hydrazine or dimethylhydrazine, the products were white involatile solids and could not be separated from the hydrochlorides. With hydrazine other reactions could also occur easily; in some experiments the diboron tetrachloride appeared to initiate violent and complete decomposition before addition, giving nitrogen and hydrogen (dimethylhydrazine also yielded methane), while in other experiments much initial decomposition of the tetrachloride occurred. Hydrolysis of the solid products of normal reactions gave very variable amounts of hydrogen, these being always much lower than theoretical; the simultaneous formation of ammonia (from the hydrazine reaction) and dimethylamine (from dimethylhydrazine) indicated reduction of the hydrochlorides. Hence it seems probable that B–B bonding did remain in the products to a considerable extent, and that

[11] Nöth, 17th Internat. Congress Pure Appl. Chem., Munich, 1959.

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these should be formulated with –N–B–B–N–N–B–B–N– chains rather than with chains containing alternate boron and nitrogen atoms.

Ethylenediamine.—This reaction followed a similar course to the hydrazine addition, with a 5 : 1 reaction ratio and a white solid product which on hydrolysis (with hydrochloride still present) gave a high recovery of hydrogen, indicating retention of B–B bonding and little reduction of the hydrochloride.

Dimethylamine.—A previous study [1] of the reaction with diboron tetrachloride gave a reaction ratio of less than 8 : 1 with tetrakis(dimethylamino)diboron as the chief product, tris(dimethylamino)borine also being formed in small amounts. The properties of the diboron compound, $B_2(NMe_2)_4$, have since been studied in more detail.[12] Of all the reactions described in this paper this was the only one to give substantial amounts of volatile products. Reaction was very slow at −78° and even after a long time at 20° less than 8 mol. of the dimethylamine had reacted. The incompleteness of reaction may be due to the very slow reaction of the intermediate $Me_2N{\cdot}BCl{\cdot}BCl{\cdot}NMe_2$ with more amine, since this intermediate did not react with dimethylaminodimethylborine [7] to give the tetra-aminoboron. After removal of the excess of dimethylamine, the volatile products were hydrolysed, and the low hydrogen evolution indicated presence of some substance not containing B–B bonds. The B : $NHMe_2$ ratio in the hydrolysate showed that $B_2(NMe_2)_4$ and $B(NMe_2)_3$ were present in the volatile fraction in approximately equimolar amounts, and this was confirmed by examination of the infrared spectrum of the fraction. Since the aminodiboron has high thermal stability [12] it is unlikely that the aminoborine could have been formed from it. There was little evidence that the diboron tetrachloride had decomposed to the extent required to provide enough boron trichloride to react with dimethylamine and form the aminoborine: some coloration due to $(BCl)_n$ was observed but this remained throughout the reaction period. It is possible that, at the stage where one dimethylamine molecule had co-ordinated and one molecule of hydrogen chloride had been eliminated to give $Me_2N{\cdot}BCl{\cdot}BCl_2$, disproportionation of the latter to boron trichloride and $(Me_2NB)_n$ might occur, with subsequent formation of the aminoborine from the trichloride, the $(Me_2NB)_n$ remaining as a solid residue. It is to be noted that certain secondary amines can effect disproportionation of boron trichloride.[13]

The results with the various donors indicate that both boron atoms in the tetrachloride have strong acceptor power, qualitatively comparable to that of boron trichloride, and there is no tendency for donation to the second boron atom to be diminished by prior donation to the first. The general stability of the adducts and the lack of reactivity towards olefins further support the idea that the reactivity of diboron tetrachloride and its ability to react with olefins are attributable to the presence of vacant orbitals on adjacent bonded atoms rather than to inherent weakness of the B–B bond.

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The University of Liverpool. [*Received, March 2nd,* 1961.]

[12] Brotherton, McCloskey, Petterson, and Steinberg, *J. Amer. Chem. Soc.*, 1960, **82**, 6242.
[13] Gerrard, Hudson, and Mooney, *J.*, 1960, 5169.

655. *Dehydrogenation with Mercuric Acetate in the Lupane Series. Part I. Betulin and Betulinic Acid.*

By J. M. Allison, William Lawrie, John McLean, and G. R. Taylor.

Mercuric acetate reacts with betulin (Ia) in chloroform–acetic acid to form the cyclic ether, 13β,28-epoxylup-20(30)-en-3β-ol (II; R = H). Under the same conditions betulin diacetate (Id) forms the non-conjugated diene, 3β,28-diacetoxylupa-12,20(30)-diene (XIV; R = Ac). Comparable reactions are undergone by acetylbetulinic acid (Ib) and methyl acetylbetulinate (Ic) which form respectively the γ-lactone 3β-acetoxylup-20(30)-en-28,13β-olide (IX), and the non-conjugated diene, methyl-3β-acetoxylupa-12,20(30)-dien-28-oate (X).

Mercuric acetate has frequently been employed as a dehydrogenating agent in the steroid field,[1] and in the references cited the reaction leads to the introduction of an ethylenic bond in conjugation with an existing double bond. Biedebach [2] extended the reaction to triterpenes and in general found that whereas α- and β-amyrin derivatives did not react with mercuric acetate in chloroform–acetic acid, derivatives of α-lupene, *viz.*, betulin and lupeol, formed dehydro-compounds of unknown constitution, and it is the purpose of the present work to describe the nature of these compounds.

Biedebach observed that the reactions of betulin and lupeol with mercuric acetate were not dependent on the presence of the alcohol group since their esters were also dehydrogenated. He established that the dehydrogenation was associated with the presence of the olefinic bond in these compounds, since the dihydro-compounds did not react with mercuric acetate. Henbest and Nicholls [3] recently described the formation of a cyclic ether by reaction of the γδ-unsaturated alcohol, bicyclo[2,2,1]hept-5-en-2α-ylmethanol, with mercuric acetate, and Brook, Rodgman, and Wright [4] describe the similar formation of a cyclic ether from the γδ-unsaturated alcohol, 2,6-dimethylhept-5-en-2-ol.

We have repeated Biedebach's experiments and find that betulin (Ia) with mercuric acetate forms a cyclic ether (II; R = H) which contains a vinylidene group (infrared bands at 1630 and 896 cm.$^{-1}$). However, since betulin may isomerise [5] in presence of acid with enlargement of ring E, there is a possibility that under the conditions of the experiment, in which acetic acid is present, ring enlargement may occur to give a compound (III; R″ = CH_2), which also contains a vinylidene group. That the cyclic ether is correctly represented by (II) is shown in the sequel.

The nuclear magnetic resonance spectrum of the ether (II; R = Ac) in carbon tetrachloride shows the following features: weak bands at +63 and +89 cycles/sec. due to C·CH_2·O protons, and peaks at +140 and +150 cycles/sec. due to Me·C= protons. There is no evidence of a 7 cycles/sec. doublet peak in the Me·C$\lesseqgtr$ region which would be expected from the Me·CH$\lesseqgtr$ methyl group in the alternative structure (III; R″ = CH_2).

Oxidation of the acetoxy-ether (II; R = Ac) with chromic acid or ozone gave the methyl ketone (IV; R = Ac, R′ = H_2) which was hydrolysed and converted into the benzoate (IV; R = Bz, R′ = H_2). The benzoate showed nuclear magnetic resonance bands at −102 and −85 cycles/sec. due to aromatic ring protons, and a peak at +131

[1] Windaus and Linsert, *Annalen*, 1928, **465**, 148; Windaus and Auhagen, *ibid.*, 1929, **472**, 185; Windaus, Riemann, and Zühlsdorff, *ibid.*, 1942, **552**, 135; Eck and Hollingsworth, *J. Amer. Chem. Soc.*, 1942, **64**, 140; Barton and Rosenfelder, *J.*, 1951, 2381; Ruyle, Jacob, Chemerda, Chamberlin, Rosenburg, Sita, Erickson, Aluminosa, and Tishler, *J. Amer. Chem. Soc.*, 1953, **75**, 2604; Saucy, Geistlich Helbling, and Heusser, *Helv. Chim. Acta*, 1954, **37**, 250.

[2] Biedebach, *Arch. Pharm.*, 1942, **280**, 304; 1943, **281**, 49.

[3] Henbest and Nicholls, *J.*, 1959, 227.

[4] Brook, Rodgman, and Wright, *J. Org. Chem.*, 1952, **17**, 988.

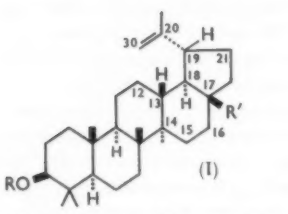
[5] Schulze and Pieroh, *Ber.*, 1922, **55**, 2332; Davy, Halsall, Jones, and Meakins, *J.*, 1951, 2702; Halsall, Jones, and Swayne, *J.*, 1954, 1902.

XUM

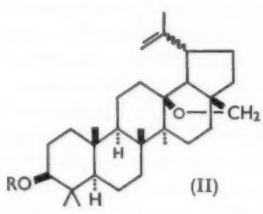
cycles/sec. due to Me·CO protons. Again there is no evidence of a 7 cycles/sec. doublet which would be expected from the alternative structure (III; R'' = O).

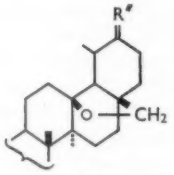
Hydrogenation of the acetoxy-ether (II; R = Ac) in presence of platinum led to the corresponding saturated ether (V; R = Ac) which on oxidation furnished the acetyl-dihydro-acid lactone (VI; R = Ac), showing the absorption at 1770 cm.$^{-1}$ of a γ-lactone. This lactone ring could terminate at position 13, 15, 19, or 21, but reduction with lithium aluminium hydride gives a triol (VII; R = H) which gave only a diacetate (VII; R = Ac). Thus it seems that one of the hydroxyl groups is tertiary and this is confirmed by ready dehydration of the diacetate with phosphorus oxychloride in pyridine to give the iso-betulin diacetate (VIII) showing absorption consistent with the presence of a trisubstituted ethylenic bond ($\lambda_{max.}$ 206 mμ, ε 7900; $\nu_{max.}$ 1650 and 3060 cm.$^{-1}$). These reactions rule out positions 15 and 21 as ends of the γ-lactone, and a decision was made between $C_{(13)}$ and $C_{(19)}$ on the basis of experiments on betulinic acid and its methyl ester.

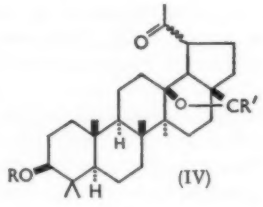
Treatment of acetylbetulinic acid (Ib) with mercuric acetate gives a γ-lactone (IX) showing infrared bands (in CCl_4) at 1792 (γ-lactone), 1736 and 1245 cm.$^{-1}$ (acetate), 1645

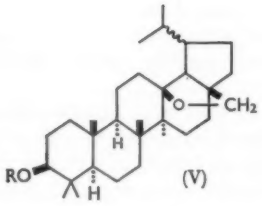


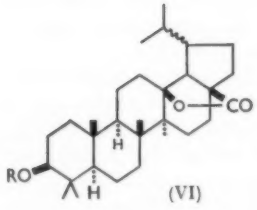
(a) R = H; R' = CH_2·OH
(b) R = Ac; R' = CO_2H
(c) R = Ac; R' = CO_2Me
(d) R = Ac; R' = CH_2·OAc

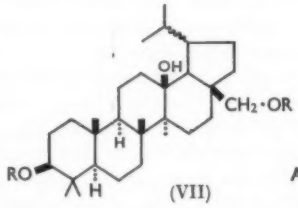


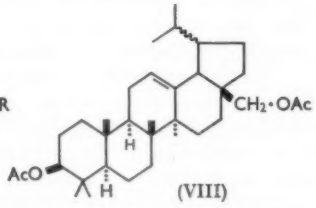












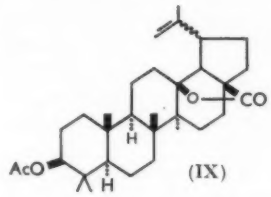
and 910 cm.$^{-1}$ (vinylidene). The presence of a vinylidene group in this compound was confirmed when ozonolysis yielded formaldehyde and the norketone (IV; R = Ac, R' = O). Hydrogenation of the lactone (IX) gives the same dihydro-lactone (VI; R = Ac) as is derived from betulin (Ia) *via* the dihydro-ether (V; R = Ac). Consequently the lactone link in the acetylbetulinic lactone (IX) terminates at the same carbon atom as the ether link in (V) or (II). For reasons stated above the lactone link in the acetylbetulinic lactone (IX) must terminate on $C_{(13)}$ or $C_{(19)}$, but the $C_{(19)}$-lactone, thurberogenin, is known;[6] hence, by elimination, the lactone link in (IX) terminates at position 13. The lactone

[6] Djerassi, Geller, and Lemin, *J. Amer. Chem. Soc.*, 1953, **75**, 2254; Djerassi, Farkas, Lui, and Thomas, *ibid.*, 1955, **77**, 5330.

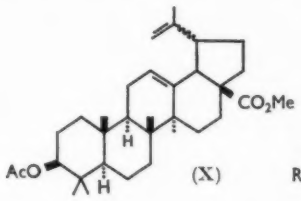
(IX) gives a very faint colour with tetranitromethane and shows very weak ultraviolet absorption at 204 mμ. Djerassi [6] reports similar behaviour for thurberogenin.

These findings were confirmed when methyl acetylbetulinate (Ic) with mercuric acetate gave the non-conjugated diene (X), $\lambda_{max.}$ 206 mμ (ε 7100), $\nu_{max.}$ 3078, 1634, 901 (>C=CH_2), 1730 and 1250 cm.$^{-1}$ (OAc). Hydrogenation (1 mol.) of the diene (X) resulted in disappearance of the vinylidene absorption in the infrared region, the product (XIa) containing a trisubstituted ethylenic bond ($\lambda_{max.}$ 205 mμ, ε 5300; $\nu_{max.}$ 816 cm.$^{-1}$). The monounsaturated ester (XIa) was hydrolysed vigorously with sodium ethoxide to the corresponding acid (XIb), which with hydrogen chloride in chloroform gave the lactone (VI; R = H).

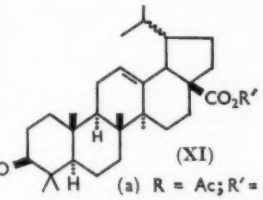
The presence of a five-membered ring E in the lactone series was demonstrated by oxidation of the unsaturated lactone (IX) with selenium dioxide to the αβ-unsaturated



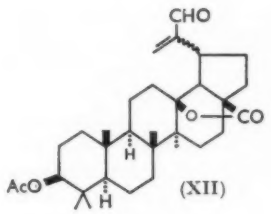
(IX)



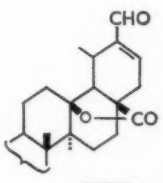
(X)



(XI)
(a) R = Ac; R′ = Me
(b) R = H, R′ = H



(XII)



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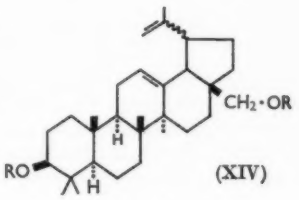
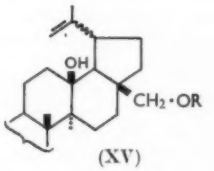


(XIV)



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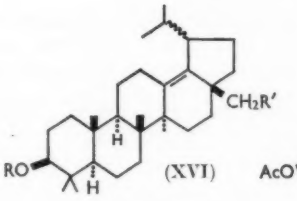
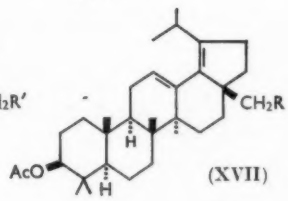
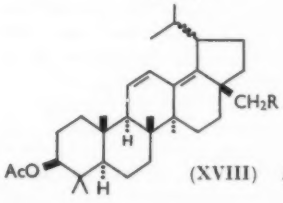


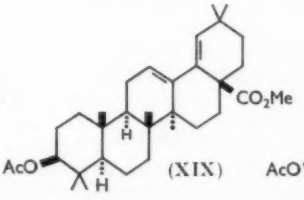
(XVI)



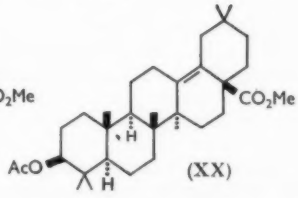
(XVII)



(XVIII)



(XIX)



(XX)

aldehyde (XII) showing absorption at 222 mμ (ε 7000). Had a six-membered ring E been present in the unsaturated lactone as in (III; R″ = CH_2) the αβ-unsaturated aldehyde (XIII) would have been formed and, being more highly substituted than (XII), would have shown absorption at 234 mμ.[6]

Betulin diacetate (Id) also reacts with mercuric acetate in chloroform–acetic acid, and gives a non-conjugated diene (XIV; R = Ac). This absorbs 1 mol. of hydrogen

catalytically, to form the isobetulin diacetate (VIII) and this forms an oxide which does not give a colour with tetranitromethane or show ethylenic absorption in the ultraviolet spectrum. The non-conjugated dienyl diacetate (XIV; R = Ac) has also been obtained from the ester (X) and from the unsaturated lactone (IX). Reduction of the ester (X) with lithium aluminium hydride in ether furnished the diol (XIV; R = H) which yielded a diacetate (XIV; R = Ac). Similar reduction of the unsaturated lactone (IX) afforded the triol (XV; R = H) which at 100° also yielded a diacetate (XV; R = Ac). The latter acetate, on dehydration with phosphorus oxychloride in pyridine, gave the diacetoxy-diene (XIV; R = Ac). The original vinylidene group of betulin diacetate is still present in this diene, which shows infrared bands at 1625 and 896 cm.$^{-1}$, but on hydrogenation of the diene the vinylidene peaks in the infrared spectrum disappear. Since isobetulin diacetate (VIII) is also obtained by dehydration of the diacetoxy-alcohol (VII; R = Ac) in which the hydroxyl group is known to be at position 13, the new ethylenic bond resulting from the action of mercuric acetate on betulin diacetate and on methyl acetylbetulinate must be at position 12, 13, or 13, 18. Of these two possibilities the former is chosen because the absorption of isobetulin diacetate (VIII) ($\lambda_{max.}$ 206 mμ, ε 7900) indicates a trisubstituted ethylenic bond, and this has been confirmed by experiments on the lupeol analogue of (VIII) in which oxidative cleavage of the double bond gives a keto-aldehyde.[7]

The isomeric unsaturated diacetate (XVI; R = Ac, R′ = OAc) containing the fully substituted 13,18-ethylenic bond has also been obtained by isomerising dehydrobetulin diacetate (XIV; R = Ac) with mineral acid to a mixture of conjugated dienes which we represent as (XVII and XVIII; R = OAc). Chromatography of the mixture afforded the pure *cisoid* heteroannular diene (XVII; R = OAc), $[\alpha]_D$ +219°, $\lambda_{max.}$ 234 mμ (ε 9400), which on hydrogenation absorbed one mol. of hydrogen to give the tetrasubstituted olefin (XVI; R = Ac, R′ = OAc), $\lambda_{max.}$ 209 mμ (ε 12,500). The constitutions ascribed to this diene and to the olefin are supported by the molecular rotation change on hydrogenation of the diene (see Table) which is similar to that which occurs when methyl isodehydro-oleanolate acetate[8] (XIX) and 3β-acetoxylupa-12,18-diene[7] (XVII; R = H) are hydrogenated.

Molecular rotation changes accompanying hydrogenation.

	$[\alpha]_D$	M_D	Δ
(XIX)[8]	+209°	+1065°	−1410°
(XX)[9]	−67·5	−345	
(XVII; R = H)[7]	+263	+1230	−1324
(XVI; R = Ac, R′ = H)[7]	−20	−94	
(XVII; R = OAc)	+219	+1145	−1371
(XVI; R = Ac, R′ = OAc)	−43	−226	

The *transoid* diene (XVIII; R = OAc) was not obtained pure, but a fraction resulting from the chromatographic separation of the conjugated dienes showed $\lambda_{max.}$ 239, 247, 256 mμ (ε 12,600, 11,800, and 6700) in keeping with the spectral properties to be expected from such a *transoid* heteroannular diene.[8]

Experimental

Rotations were determined for chloroform solutions at room temperature, ultraviolet spectra for ethanol solutions, and infrared spectra for Nujol mulls unless otherwise stated. Light petroleum refers to the fraction of b. p. 60—80°.

13β,28-*Epoxylup*-20(30)-*en*-3β-*ol* (II; R = H).—Betulin (1 g.) in warm chloroform (30 ml.) was heated for 3 hr. on the steam-bath with mercuric acetate (17 g.) in glacial acetic acid (370 ml.). The solution was cooled, filtered from mercurous acetate, and poured into water.

[7] To be described in Part II of this series.
[8] Barton and Brooks, *J.*, 1951, 257.
[9] Jeger, Norymberski, and Ruzicka, *Helv. Chim. Acta*, 1944, **27**, 1532.

XUM

Extraction with chloroform (2 × 100 ml.), washing of the extract, and removal of solvent gave the mercury complex which was dissolved in ethyl acetate (150 ml.) and treated with hydrogen sulphide for 3 hr. The suspension was filtered from mercuric sulphide and taken to dryness, and the residue in ether–methanol (19 : 1) filtered successively through kieselguhr and alumina. The yellow gum (0·86 g.) obtained on removal of solvent was chromatographed in ether on alumina (15 g.). Elution with ether gave 13β,28-*epoxylup*-20(30)-*en*-3β-*ol* (0·535 g.), needles (from methylene chloride–light petroleum), m. p. 266°, $[\alpha]_D$ +60° (*c* 1·4), $\nu_{max.}$ 3460 cm.$^{-1}$ (OH) 1620 and 893 cm.$^{-1}$ (vinylidene) (Found: C, 81·5; H, 11·1. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%).

The *acetate* (II; R = Ac), obtained by treating the alcohol with acetic anhydride in pyridine at 100°, formed needles (from chloroform–methanol), m. p. 242—244°, $[\alpha]_D$ +64° (*c* 1·2), $\nu_{max.}$ 1730 and 1250 cm.$^{-1}$ (OAc), 1630 and 896 cm.$^{-1}$ (vinylidene), $\lambda_{max.}$ 206 mμ (ε 6000) (Found: C, 79·2; H, 10·6. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·4%).

This acetate was also prepared by refluxing betulin 3-acetate (0·75 g.) in chloroform (50 ml.) for 5 hr. with mercuric acetate (25 g.) in acetic acid (400 ml.). Working up as above, followed by chromatography on alumina (15 g.) and elution with benzene, gave the acetate (0·25 g.), m. p. and mixed m. p. (with the specimen prepared as above) 242—244°. The infrared spectra of the acetates were identical.

3β-*Acetoxy*-13β,28-*epoxylupane* (V; R = Ac).—A solution of 3β-acetoxy-13β,28-epoxylup-20(30)-ene (0·21 g.) in ether (150 ml.) containing acetic acid (10 ml.) was hydrogenated in presence of platinum oxide (0·15 g.) for 12 hr. Working up in the usual way gave 3β-*acetoxy*-13β,28-*epoxylupane*, needles (0·18 g.) (from chloroform–methanol), m. p. 281—282° (*in vacuo*), $[\alpha]_D$ +48° (*c* 1·5), $\nu_{max.}$ 1734 and 1248 cm.$^{-1}$ (OAc) (no selective absorption in the ultraviolet range 200—210 mμ, and no colour with tetranitromethane) (Found: C, 79·4; H, 11·1. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). Hydrolysis of the acetate (0·7 g.) with boiling methanolic 5% potassium hydroxide (200 ml.) for 1·5 hr. and isolation of the product through ether gave 13β,28-*epoxylupan*-3β-*ol* (V; R = H) (0·6 g.), needles (from methylene chloride–acetone), m. p. 213°, $[\alpha]_D$ +40° (*c* 1·4), $\nu_{max.}$ 3320 cm.$^{-1}$ (OH) (Found: C, 81·4; H, 11·3. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). When treated with a 6% solution of hydrogen peroxide in 100% formic acid oxide formation did not occur, thereby confirming the absence of a double bond; instead, the 3β-*formate* (V; R = CHO) was isolated, as plates (from chloroform–methanol), m. p. 254—255°, $[\alpha]_D$ +49·5 (*c* 1·1), $\nu_{max.}$ 1700 and 1175 cm.$^{-1}$ (formate) (Found: C, 78·8; H, 11·0. $C_{31}H_{50}O_3$ requires C, 79·1; H, 10·7%). Hydrolysis of the formate with methanolic potassium hydroxide re-formed the alcohol (V; R = H).

13β,28-*Epoxylupan*-3-*one*.—Oxidation of 13β,28-epoxylupan-3β-ol (0·38 g.) in pyridine (30 ml.) with chromium trioxide (0·3 g.) in pyridine (40 ml.) at room temperature (20 hr.) and isolation of the product in the usual way gave 13β,28-*epoxylupan*-3-*one*. The ketone (0·27 g.), purified by elution from alumina with benzene–light petroleum (1 : 1) and crystallised from chloroform–methanol, had m. p. 252—253° (*in vacuo*), $[\alpha]_D$ +68° (*c* 1·1), $\nu_{max.}$ 1700 cm.$^{-1}$ (C=O) (Found: C, 80·4; H, 10·9. $C_{30}H_{48}O_2,\frac{1}{2}CH_3{\cdot}OH$ requires C, 80·2; H, 11·0%).

3β,28-*Diacetoxylupa*-12,20(30)-*diene* (XIV; R = Ac).—Betulin diacetate (1 g.) in chloroform (20 ml.) was treated with mercuric acetate in acetic acid as described above for betulin. The product was dissolved in benzene and filtered through alumina (50 g.). Removal of benzene gave a gum which deposited the *diacetate* (XIV; R = Ac) (0·15 g.) that formed needles (from aqueous ethanol), m. p. 177—178°, $[\alpha]_D$ +41° (*c* 3·4), $\nu_{max.}$ 1730, 1256, and 1240 cm.$^{-1}$ (OAc) 1625 and 896 cm.$^{-1}$ (vinylidene), $\lambda_{max.}$ 204 mμ (ε 8000) (Found: C, 77·9; H, 9·9. $C_{34}H_{52}O_4$ requires C, 77·8; H, 10·0%). Hydrolysis of this diacetate with boiling methanolic 5% potassium hydroxide for 1·5 hr. and isolation of the product through ether in the absence of mineral acid gave *lupa*-12,20(30)-*diene*-3β,28-*diol* (XIV; R = H), needles (from chloroform–light petroleum), m. p. 196—198° with resolidification and remelting at 211—214°, $[\alpha]_D$ +8° (*c* 1·1), $\nu_{max.}$ 3220 cm.$^{-1}$ (OH), 1620 and 885 cm.$^{-1}$ (vinylidene). This diol was also obtained by reduction of the ester (X) with lithium aluminium hydride; similar reduction of the unsaturated lactone (IX), followed by acetylation and dehydration, gave the corresponding diacetate (XIV; R = Ac).

3β,28-*Diacetoxylup*-12-*ene* (VIII).—Hydrogenation of the diacetate (XIV; R = Ac) (0·9 g.) in ether (200 ml.) containing acetic acid (20 ml.) in presence of platinum oxide (0·5 g.) for 15 hr. gave the *diacetate* (VIII), needles (from chloroform–methanol), m. p. 209—210°, $[\alpha]_D$ +16° (*c* 1·2), $\nu_{max.}$ 1730 and 1240 cm.$^{-1}$ (OAc), $\lambda_{max.}$ 206 mμ (ε 7900) (Found: C, 77·5; H, 10·5.

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$C_{34}H_{54}O_4$ requires C, 77·5; H, 10·3%). This compound was also prepared by dehydration of the triol diacetate (VII; R = Ac) which is described below. Hydrolysis of the diacetate with methanolic potassium hydroxide and working up through ether gave *lup*-12-*ene*-3β,28-*diol*, needles (from chloroform–methanol), m. p. 214—217°, $[\alpha]_D$ −14° (*c* 1·1) (Found: C, 81·3; H, 11·6. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%).

3β,28-*Diacetoxy*-12,13-*epoxylupane*.—A solution of the diacetate (VIII) (0·19 g.) in ethyl acetate (15 ml.) was treated with 30% hydrogen peroxide (3 ml.) in 100% formic acid (15 ml.) at 45° for 1·5 hr. Working up through ether gave the *epoxide* (0·11 g.), needles (from methanol), m. p. 207—208°, $[\alpha]_D$ +22° (*c* 1·1) (Found: C, 75·3; H, 10·2. $C_{34}H_{54}O_5$ requires C, 75·2; H, 10·0%). The epoxide was transparent to ultraviolet light and did not give a colour with tetranitromethane.

3β-*Acetoxylupan*-28,13β-*olide* (VI; R = Ac).—To a boiling solution of 3β-acetoxy-13β,28-epoxylupane (V; R = Ac) (0·5 g.) in acetic acid (50 ml.), chromium trioxide (1 g.) in acetic acid (150 ml.) was added during 20 min., and this mixture was refluxed for 1·5 hr. Excess of chromic acid was destroyed with methanol, and the product worked up through ether to give 3β-*acetoxylupan*-28,13β-*olide* (VI; R = Ac), plates (0·47 g.) (from chloroform–methanol), m. p. 299—300°, $[\alpha]_D$ +49° (*c* 1·1), $\nu_{max.}$ 1734 and 1250 cm.$^{-1}$ (OAc) 1770 cm.$^{-1}$ (γ-lactone) (Found: C, 76·85; H, 10·2. $C_{32}H_{50}O_4$ requires C, 77·1; H, 10·1%).

Lupane-3β,13β,28-*triol* (VII; R = H).—The lactone (VI; R = Ac) (0·25 g.) in dry ether (200 ml.) was refluxed with lithium aluminium hydride (1 g.) for 1·5 hr. Isolation of the product through ether gave the *triol* (VII; R = H), needles (0·2 g.) (from chloroform–benzene), m. p. 240—242° (decomp.), $[\alpha]_D$ +22° (*c* 1·0 in ethanol–chloroform), $\nu_{max.}$ 3220 cm.$^{-1}$ (OH) (Found: C, 78·0; H, 11·2. $C_{30}H_{52}O_3$ requires C, 78·2; H, 11·4%). Acetylation of the triol (VII; R = H) with acetic anhydride and pyridine at 100° gave 3β,28-*diacetoxylupan*-13β-*ol* (VII; R = Ac), needles (from methanol), m. p. 272—273°, $[\alpha]_D$ +19° (*c* 1·0), $\nu_{max.}$ 3470 cm.$^{-1}$ (OH), 1745, 1712, and 1242 cm.$^{-1}$ (OAc) (Found: C, 75·3; H, 10·0. $C_{34}H_{56}O_5$ requires C, 74·95; H, 10·4%). Dehydration of this diacetate (0·08 g.) in dry pyridine (15 ml.) with phosphorus oxychloride (4 ml.) at 100° for 1·5 hr. and working up through ether gave the diacetate (VIII), needles (0·05 g.) (from chloroform–methanol), m. p. 210°, $[\alpha]_D$ +18° (*c* 1·3). The latter diacetate did not depress the m. p. of that prepared as above by hydrogenation of the diacetate (XIV; R = Ac), and the compounds showed infrared identity.

3β-*Acetoxy*-13β,28-*epoxy*-30-*norlupan*-20-*one* (IV; R = Ac, R′ = H_2).—(*a*) 3β-Acetoxy-13β,28 epoxylup-20(30)-ene (II; R = Ac) (0·41 g.) in methylene chloride (60 ml.) was ozonised at −45° for 35 min. The mixture was allowed to reach room temperature, then acetic acid (15 ml.) and zinc dust (1 g.) were added during 20 min. with stirring, which was continued for a further 40 min. The suspension was filtered and the product isolated by washing the filtrate, drying (Na_2SO_4), and evaporation to dryness. 3β-*Acetoxy*-13β,28-*epoxy*-30-*norlupan*-20-*one* crystallised from chloroform–methanol as plates (0·28 g.), m. p. 317—319°, $[\alpha]_D$ +3° (*c* 1·3), $\nu_{max.}$ 1736 and 1245 cm.$^{-1}$ (OAc) and 1706 cm.$^{-1}$ (C=O) (Found: C, 77·1; H, 10·1. $C_{31}H_{48}O_4$ requires C, 76·8; H, 10·0%).

(*b*) The ketone was also obtained by oxidation of 3β-acetoxy-13β,28-epoxylup-20(30)-ene (II; R = Ac) (2·31 g.) in boiling acetic acid by slow addition of chromium trioxide (7 g.) in acetic acid (80 ml.) followed by boiling under reflux for 1·5 hr. The excess of chromic acid was destroyed with methanol and on working up through ether a gum was obtained. Chromatography on alumina (20 g.) and elution with benzene–light petroleum (1 : 1) gave the ketone (IV; R = Ac, R′ = H_2) (0·31 g.), m. p. 317—319°, $[\alpha]_D$ +4° (*c* 1·3).

3β-*Benzoyloxy*-13β,28-*epoxy*-30-*norlupan*-20-*one* (IV; R = Bz, R′ = H_2).—Hydrolysis of the acetoxy-norketone (IV; R = Ac, R′ = H_2) gave an amorphous alcohol that (0·56 g.) with benzoyl chloride (2 ml.) in pyridine (30 ml.) at 100° (1·5 hr.) gave, after working up through ether followed by chromatography on alumina and elution with benzene–light petroleum (1 : 1), the *benzoate* (IV; R = Bz, R′ = H_2), needles (0·51 g.) (from chloroform–methanol), m. p. 313°, $[\alpha]_D$ +26·5° (*c* 1·5), $\nu_{max.}$ 1725, 1280, and 1120 cm.$^{-1}$ (benzoate) (Found: C, 76·7; H, 9·2. $C_{36}H_{50}O_4$,CH_3·OH requires C, 76·8; H, 9·4%).

3β-*Acetoxylup*-20(30)-*en*-28,13β-*olide* (IX).—Acetylbetulinic acid (0·5 g.) in chloroform (15 ml.) was heated at 100° with a solution of mercuric acetate (7 g.) in acetic acid for 5 hr. The product was worked up through chloroform, the chloroform solution being washed, dried ($CaCl_2$), and treated with hydrogen sulphide (3 hr.). Filtration and removal of solvent gave a gum which still contained a trace of mercury. The latter was removed by taking up the

product in pyridine and again passing hydrogen sulphide. Filtration and removal of pyridine gave a solid which was chromatographed on alumina (15 g.). Elution with light petroleum–benzene (2 : 1) gave sulphur followed by 3β-*acetoxylup*-20(30)-*en*-28,13β-*olide* (IX), needles (0·26 g.) (from chloroform–methanol), m. p. 315—317°, $[\alpha]_D$ +60° (*c* 1·1), $\nu_{max.}$ 1786 cm.$^{-1}$ (γ-lactone), 1739 and 1245 cm.$^{-1}$ (OAc), 1630 and 913 cm.$^{-1}$ (vinylidene). There was weak absorption at 204 mμ (ε 2000) and the compound did not give a colour with tetranitromethane [6] (Found: C, 77·1; H, 9·8. $C_{32}H_{48}O_4$ requires C, 77·4; H, 9·7%).

Hydrogenation of the lactone (IX) (0·15 g.) in acetic acid (100 ml.) containing platinum oxide (0·05 g.) for 20 hr. and working up as usual gave the saturated acetyl-lactone (VI; R = Ac), plates (0·12 g.) (from chloroform–methanol), m. p. 301—302°, $[\alpha]_D$ +46° (*c* 1·78) (Found: C, 77·4; H, 10·2. Calc. for $C_{32}H_{50}O_4$: C, 77·1; H, 10·1%). The m. p. did not depress that of the saturated lactone acetate obtained from the ether (V; R = Ac), and the compounds showed infrared identity.

Boiling the lactone (IX) (0·309 g.) in benzene (5 ml.) with methanolic 5% potassium hydroxide (55 ml.) for 3 hr. and working up through ether gave 3β-*hydroxylup*-20(30)-*en*-28,13β-*olide* needles (from methanol), m. p. 308—309° (*in vacuo*), $[\alpha]_D$ +57° (*c* 1·0), $\nu_{max.}$ 3436 cm.$^{-1}$ (OH), 1776 cm.$^{-1}$ (γ-lactone), 1639 and 893 cm.$^{-1}$ (vinylidene) (no appreciable ultraviolet absorption) (Found: C, 79·0; H, 10·3. $C_{30}H_{48}O_3$ requires C, 79·2; H, 10·2%). Hydrogenation of this lactone (0·103 g.) in acetic acid (100 ml.) in presence of platinum oxide (0·1 g.) for 12 hr. gave 3β-*hydroxylupan*-28,13β-*olide* (VI; R = H) needles (0·07 g.) (from methanol), m. p. 314—316°, $[\alpha]_D$ +41° (*c* 1·06), $\nu_{max.}$ 1767 cm.$^{-1}$ (γ-lactone) (Found: C, 78·7; H, 10·6. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%).

Ozonolysis of 3β-*Acetoxylup*-20(30)-*en*-28,13β-*olide* (IX).—The lactone (0·22 g.) in chloroform (20 ml.) was ozonised at −45° for 45 min. When the solution had reached room temperature, acetic acid (4 ml.) was added, followed by zinc dust (1 g.) with stirring during 20 min. The solution was stirred for a further 40 min., filtered, and diluted with chloroform (75 ml.), and the chloroform layer was washed with water (3 × 50 ml.). The combined washings were treated with a cold saturated aqueous solution of dimedone and, after 48 hr., the resultant precipitate was collected and recrystallised from methanol to give formaldehyde dimethone as needles (0·06 g., 45%), m. p. and mixed m. p. 190—191°. Evaporation of the dried (Na_2SO_4) chloroform solution and crystallisation of the residue (0·195 g.) from ethanol gave 3β-*acetoxy*-20-*oxo*-30-*norlupan*-28,13β-*olide* (IV; R = Ac, R′ = O), plates, m. p. 317—319° (*in vacuo*), $[\alpha]_D$ +2° (*c* 2·3), $\nu_{max.}$ 1786 (γ-lactone), 1733 and 1247 (OAc), and 1715 cm.$^{-1}$ (C=O) (Found: C, 74·8; H, 9·5. $C_{31}H_{46}O_5$ requires C, 74·7; H, 9·3%).

3β-*Acetoxy*-29-*oxolup*-20(30)-*en*-28,13β-*olide* (XII).—A solution of the acetoxy-lactone (IX) (0·203 g.) in acetic acid (10 ml.) was refluxed with selenium dioxide (0·35 g.) for 2 hr. Filtration and evaporation followed by chromatography on alumina (10 g.) from benzene–light petroleum (1 : 1) gave the *aldehyde* (XII), needles (0·16 g.) (from methanol), m. p. 312—314° (*in vacuo*), $[\alpha]_D$ +46·5° (*c* 1·25), $\nu_{max.}$ 1779 (γ-lactone), 1730 and 1242 (OAc), and 1692 cm.$^{-1}$ (αβ-unsaturated aldehyde), $\lambda_{max.}$ 222 mμ (ε 6800) (Found: C, 75·3; H, 9·2. $C_{32}H_{46}O_5$ requires C, 75·3; H, 9·1%).

Lup-20(30)-*ene*-3β,13β,28-*triol* (XV; R = H).—The lactone (IX) (2 g.) in benzene–ether (1 : 4; 500 ml.) was refluxed with lithium aluminium hydride (2 g.) for 1·5 hr. Isolation through ether, without contact with mineral acid, gave the *triol* (XV; R = H) (1·98 g.) prisms (from aqueous methanol), m. p. 204—206°, $[\alpha]_D$ +49° (*c* 1·75), $\lambda_{max.}$ 204 mμ (ε 3500), $\nu_{max.}$ 3356 (OH), 1647 and 893 cm.$^{-1}$ (vinylidene) (Found: C, 75·9; H, 11·0. $C_{30}H_{50}O_3$,CH_3·OH requires C, 75·9; H, 11·1%). Treatment with acetic anhydride in pyridine, at room temperature for 48 hr. or at 100° for 3 hr., afforded 3β,28-*diacetoxylup*-20(30)-*en*-13β-*ol* (XV; R = Ac), blades (from chloroform–methanol), m. p. 228—230°, $[\alpha]_D$ +44° (*c* 1·93), $\lambda_{max.}$ 205 mμ (ε 3900), $\nu_{max.}$ 3460 (OH), 1739, 1712, and 1254 (OAc), and 1645 and 884 cm.$^{-1}$ (vinylidene) (Found: C, 75·3; H, 10·1. $C_{34}H_{54}O_5$ requires C, 75·2; H, 10·0%). Dehydration of this acetate (1 g.) in dry pyridine (60 ml.) with phosphorus oxychloride (8 ml.) at 100° for 3 hr. and working up through ether gave 3β,28-diacetoxylupa-12,20(30)-diene (XIV; R = Ac), plates (from ethanol), m. p. and mixed m. p. 177—179°, $[\alpha]_D$ +40° (*c* 2·6).

Methyl 3β-*Acetoxylupa*-12,20(30)-*dien*-28-*oate* (X).—Methyl acetylbetulinate (4·85 g.) in chloroform (200 ml.) was refluxed with mercuric acetate (70 g.) in acetic acid (1 l.) for 5 hr. Working up through chloroform gave a product which was freed from mercury by dissolution in pyridine and passage of hydrogen sulphide for 3 hr. Filtration, removal of pyridine, and

XUM

chromatography on alumina (100 g.) from light petroleum–benzene (1 : 3) gave the *ester* (X), prisms (1·42 g.) (from methanol), m. p. 217—219°, $[\alpha]_D$ +60° (*c* 3·54), $\nu_{max.}$ 1739 and 1253 (ester), 1631 and 885 cm.$^{-1}$ (vinylidene), $\lambda_{max.}$ 206 mμ (ε 7100) (Found: C, 77·5; H, 10·2. $C_{33}H_{50}O_4$ requires C, 77·6; H, 9·9%).

Methyl 3β-*Hydroxylupa*-12,20(30)-*dien*-28-*oate*.—Hydrolysis of the ester (X) (0·2 g.) with boiling methanolic 3% potassium hydroxide (50 ml.) for 3 hr. and isolation in the usual way gave *methyl* 3β-*hydroxylupa*-12,20(30)-*dien*-28-*oate* (0·17 g.), needles (from aqueous methanol), m. p. 182—184°, $[\alpha]_D$ +45° (*c* 1·1), $\lambda_{max.}$ 207 mμ (ε 6300), $\nu_{max.}$ 3571 (OH), 1718 (ester), 1637, and 893 cm.$^{-1}$ (vinylidene) (Found: C, 79·4; H, 10·5. $C_{31}H_{48}O_3$ requires C, 79·4; H, 10·3%).

3β-*Hydroxylupa*-12,20(30)-*dien*-28-*oic Acid*.—Hydrolysis of the ester (X) (0·9 g.) in ethanol (30 ml.) containing sodium (1 g.) in a sealed tube at 200° for 19 hr. and isolation in the usual way gave the *hydroxy-acid* (0·29 g.), needles (from methanol), m. p. 289—291° (*in vacuo*), $[\alpha]_D$ +61° (*c* 0·54), $\lambda_{max.}$ 206 mμ (ε 6600), $\nu_{max.}$ 3436 (OH), 1701 and 1678 (CO_2H), 1638 and 891 cm.$^{-1}$ (vinylidene) (Found: C, 78·0; H, 10·2. $C_{30}H_{48}O_3,\frac{1}{2}CH_3{\cdot}OH$ requires C, 77·8; H, 10·3%). With acetic anhydride in pyridine this gave 3β-*acetoxylupa*-12,20(30)-*dien*-28-*oic acid*, plates (from aqueous methanol), m. p. 280—282° (*in vacuo*), $[\alpha]_D$ +68° (*c* 0·6) (Found: C, 76·4; H, 9·9. $C_{32}H_{48}O_4,\frac{1}{2}CH_3{\cdot}OH$ requires C, 76·1; H, 9·8%). This acetoxy-acid with diazomethane regenerated the ester (X).

Reduction of Methyl 3β-*Acetoxylupa*-12,20(30)-*dien*-28-*oate* (X) *with Lithium Aluminium Hydride*.—The ester (X) (0·3 g.) in ether (50 ml.) was refluxed with lithium aluminium hydride (0·2 g.) for 1·5 hr. Working up through ether without contact with mineral acid gave, after several recrystallisations from methanol, lupa-12,20(30)-diene-3β,28-diol (XIV; R = H) (0·21 g.) showing m. p. and infrared and rotational characteristics identical with those of the sample prepared by hydrolysis of the diacetoxy-diene (XIV; R = Ac).

Methyl 3β-*Acetoxylup*-12-*en*-28-*oate* (XIa).—Hydrogenation of the ester (X) (0·23 g.) in ethyl acetate–acetic acid (1 : 5; 150 ml.) in presence of platinum oxide (0·05 g.) for 20 hr. and working up as usual gave *methyl* 3β-*acetoxylup*-12-*en*-28-*oate* (XIa), plates (0·21 g.) (from chloroform–methanol), m. p. 215—217°, $[\alpha]_D$ +19° (*c* 1·14), $\nu_{max.}$ 1739 and 1250 cm.$^{-1}$ (ester), $\lambda_{max.}$ 205 mμ (ε 5300). There was no infrared vinylidene absorption, and the compound gave a pale yellow colour with tetranitromethane (Found: C, 77·6; H, 10·2. $C_{33}H_{52}O_4$ requires C, 77·3; H, 10·2%).

3β-*Hydroxylup*-12-*en*-28-*oic Acid* (XIb).—The methyl acetoxy-ester (XIa) (0·17 g.) in ethanol (7 ml.) containing sodium (0·2 g.) was hydrolysed at 200° in an autoclave (17 hr.). Working up through ether, extraction with potassium hydroxide, and acidification gave 3β-*hydroxylup*-12-*en*-28-*oic acid* (XIb), needles (from chloroform–methanol), m. p. 287—289°, $[\alpha]_D$ +11° (*c* 1·02), $\nu_{max.}$ 3425 and 3268 (OH), and 1690 cm.$^{-1}$ (CO_2H), $\lambda_{max.}$ 206 mμ (ε 4600), giving a pale yellow colour with tetranitromethane (Found: C, 77·3; H, 10·8. $C_{30}H_{48}O_3,\frac{1}{2}CH_3{\cdot}OH$ requires C, 77·5; H, 10·7%), whose 3β-*acetate* formed plates (from aqueous methanol), m. p. 294—295° (*in vacuo*), $[\alpha]_D$ +31° (*c* 0·7), $\nu_{max.}$ 1739 and 1245 (OAc), and 1690 cm.$^{-1}$ (CO_2H) (Found: C, 77·2; H, 10·3. $C_{32}H_{50}O_4$ requires C, 77·1; H, 10·1%).

Lactonisation of the Hydroxy-acid (XIb).—The hydroxy-acid (XIb) (0·02 g.) in chloroform was treated with dry hydrogen chloride for 45 min. Removal of chloroform followed by chromatography of the residue from benzene–ether (1 : 1) on alumina (2 g.) gave 3β-hydroxylupan-28,13β-olide (VI; R = H) (0·017 g.), needles (from methanol), m. p. and mixed m. p. (with the sample described above), 313—315° (*in vacuo*), $[\alpha]_D$ +41·5° (*c* 0·36). The infrared spectra of both samples were identical.

3β,28-*Diacetoxylupa*-12,18-*diene* (XVII; R = OAc).—The non-conjugated diene diacetate (XIV; R = Ac) (1·03 g.) in acetic acid (50 ml.) containing concentrated hydrochloric acid (2 ml.) was heated to 100° for 30 min. The solution, which had become dark blue, was evaporated (*in vacuo*) and the gummy residue chromatographed from light petroleum (50 ml.) on alumina (40 g.). Elution with light petroleum (100 ml.) gave a fraction (0·14 g.), blades (from methanol), m. p. 173—200°, $[\alpha]_D$ +141·5° (*c* 0·75). This material could not be purified by further crystallisation, but spectroscopic data [$\lambda_{max.}$ 239, 247, 256 mμ (ε 12,600, 11,750, 6700)] indicate the presence of a *transoid* heteroannular diene, presumably (XVIII; R = OAc). Continued elution with light petroleum (300 ml.) gave 3β,28-*diacetoxylupa*-12,18-*diene* (XVII; R = OAc) (0·22 g.), plates (from methanol), m. p. 140—143°, $[\alpha]_D$ +219° (*c* 0·8), $\lambda_{max.}$ 234 mμ (ε 9400) (Found: C, 77·7; H, 10·2. $C_{34}H_{52}O_4$ requires C, 77·8; H, 10·0%).

3β,28-*Diacetoxylup*-13(18)-*ene* (XVI; R = Ac, R′ = OAc).—The conjugated diene diacetate

(XVII; R = OAc) (0·08 g.) in acetic acid (100 ml.) was hydrogenated in presence of platinum oxide (0·1 g.) for 20 hr. The solvent was removed *in vacuo*, and the residue (0·08 g.) was chromatographed from light petroleum (50 ml.) on alumina (6 g.). Elution with light petroleum (80 ml.) gave fractions (0·01 g.) which failed to crystallise, but further elution with the same solvent (150 ml.) gave 3β,28-*diacetoxylup*-13(18)-*ene* (0·06 g.), needles (from acetone), m. p. 158—160°, $[\alpha]_D$ −43° (*c* 1·67), $\lambda_{max.}$ 209 mμ (ε 12,500) (Found: C, 77·8; H, 10·4. $C_{34}H_{54}O_4$ requires C, 77·5; H, 10·3%).

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656. *Polycyclic Systems. Part IX.*[1] *A New Synthesis of Indeno(2′,3′ : 1,2)phenanthrene.**

By D. NASIPURI and D. N. ROY.

A new synthesis of indeno(2′,3′:1,2)phenanthrene by the application of Robinson–Mannich base ring-extension procedure to methyl 3′-oxo-1,2-cyclopentenophenanthrene-4-carboxylate (III; R = H) is described. The latter is obtained from 2-1′-naphthylethyl bromide and ethyl β-oxoadipate by successive alkylation, Bougault cyclisation, aromatisation, and Dieckmann condensation. The method with appropriate variation affords a convenient route to analogues especially suited to synthesis of compounds obtained as minor products during the dehydrogenation of steroids.

SEVERAL indeno(2′,3′:1,2)phenanthrene derivatives have been isolated as minor products on dehydrogenation of various steroidal compounds, *e.g.*, cholesterol,[2] ergosterol,[3] phytosterols,[4] and bile acids.[5] Recently, another hydrocarbon of uncertain identity but probably containing the same ring system has been reported in connection with helvolic acid.[6] There is, however, no satisfactory mechanism as yet, which can explain the formation of these hydrocarbons from steroids, the obvious cyclisation of the steroid side-chain with the original D-ring[7] having been disproved by the synthetic experiments of Cook *et al.*[8] In fact, except for the 4′-methyl derivative from cholic acid and the 6′-methyl derivative from strophanthidin,[9] the hydrocarbons are still not conclusively identified, although from the study of the absorption spectra and other physical and chemical properties, they are best to be represented as indeno(2′,3′:1,2)phenanthrenes.[8,10] An alternative mechanism proposed by Bergmann,[9] involving the opening of ring D and formation of a new five-membered ring in its place with the inclusion of the angular 13-methyl group, explains the formation of the 6′-methyl derivative from strophanthidin, but cannot be generally accepted in absence of further synthetic proof. The classical

* A preliminary account of this work appeared in *Science and Culture*, 1956, **22**, 232.

[1] Part VIII, Nasipuri, Roy, and Rakshit, *J. Indian Chem. Soc.*, 1960, **37**, 369.
[2] Diels, Gädke, and Körding, *Annalen*, 1927, **459**, 1.
[3] Diels and Karstens, *Annalen*, 1930, **478**, 129; Ruzicka, Goldberg, and Thomann, *Helv. Chim. Acta*, 1933, **16**, 812; Ruzicka and Goldberg, *ibid.*, 1935, **18**, 434; Diels and Stephan, *Annalen*, 1937, **527**, 279.
[4] Ruzicka and Goldberg, *Helv. Chim. Acta*, 1937, **20**, 1245.
[5] Ruzicka, Thomann, Brandenberger, Furter, and Goldberg, *Helv. Chim. Acta*, 1934, **17**, 200.
[6] Cram and Allinger, *J. Amer. Chem. Soc.*, 1956, **78**, 5278.
[7] Rosenheim and King, *Chem. and Ind.*, 1933, **52**, 299.
[8] Cook, Hewett, Mayneord, and Roe, *J.*, 1934, 1927.
[9] Bergmann, *J. Amer. Chem. Soc.*, 1938, **60**, 2306.
[10] Cook, Dansi, Hewett, Iball, Mayneord, and Roe, *J.*, 1935, 1319.

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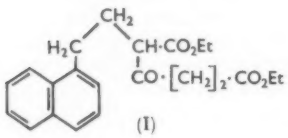
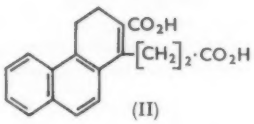
methods for the synthesis of this ring system are few and require generally inaccessible starting materials. Besides, they involve, in one step or other, intramolecular cyclisation requiring prolonged treatment with anhydrous aluminium chloride, a process which might cause the migration of alkyl groups.[11] A more reliable method is, therefore, desirable. The present communication describes a new synthesis on lines similar to those followed in our laboratory for the synthesis of alkylpicenes.[12]

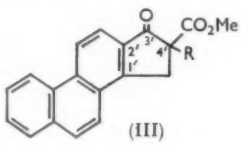
The method consists in condensation of the methiodide of a suitable Mannich base with the sodio-derivative of methyl-3′-oxo-1,2-cyclopentenophenanthrene-4′-carboxylate (III; R = H) and cyclisation of the resulting dioxo-ester to the unsaturated ketone (V) which is then easily converted into the aromatic system (VI). In order to prepare the desired β-oxo-ester (III; R = H), ethyl β-oxoadipate [13] was treated with 2-1′-naphthylethyl bromide and the crude product (I) was cyclodehydrated with concentrated sulphuric acid to give β-(2-carboxy-3,4-dihydro-1-phenanthryl)propionic acid (II). This was dehydrogenated to the corresponding aromatic acid, whose dimethyl ester was submitted to Dieckmann cyclisation. The sodio-derivative of the β-oxo-ester (III; R = H), thus obtained, was treated *in situ* with a cold methanolic solution of 4-piperidinobutan-2-one methiodide.[14] The ester (III; R = ·CH_2·CH_2·COMe) was isolated from the reaction mixture in about 70% yield and hydrolysed by a refluxing mixture of glacial acetic acid and hydrochloric acid to the pentacyclic ketone (V; R = H) in an excellent yield. The ketone was smoothly reduced with lithium aluminium hydride and subsequently dehydrated and dehydrogenated to indeno(2′,3′:1,2)phenanthrene (VI; R = R′ = R″ = H) by heating it with 30% palladium–charcoal,[15] the total over-all yield being 10—12%.



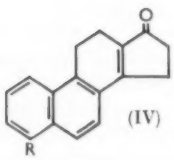
(I)



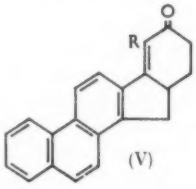
(II)



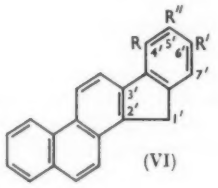
(III)



(IV)



(V)



(VI)

The ketone (IV; R = H) and its aromatic analogue were prepared by Dieckmann cyclisation of the dialkyl ester of appropriate acid (as II) and found to be identical with the ketones obtained by Bardhan [13a] and Bachmann *et al.*,[16] respectively. In a similar way, 2-(5-methyl-1-naphthyl)ethyl bromide [17] was converted into 3,4-dihydro-8-methyl-3′-oxo-1,2-cyclopentenophenanthrene (IV; R = Me) which had been prepared by Woodward *et al.*[18] by another method.

[11] Thomas, "Anhydrous Aluminium Chloride in Organic Chemistry," Reinhold Publ. Co., New York, 1941, pp. 77—94; Price and Adams, "Organic Reactions," John Wiley & Sons, Inc., New York, 1947, Vol. III, pp. 9—10.
[12] Nasipuri, *J.*, 1958, 2618, 4192; Nasipuri and Roy, *J. Indian Chem. Soc.*, 1959, **36**, 817.
[13] (*a*) Bardhan, *J.*, 1936, 1848; (*b*) Guha, Rakshit, and Nasipuri, *J. Indian Chem. Soc.*, 1960, **37**, 267.
[14] Wilds and Werth, *J. Org. Chem.*, 1952, **17**, 1149.
[15] Linstead and Thomas, *J.*, 1940, 1127.
[16] Bachmann and Kloetzel, *J. Amer. Chem. Soc.*, 1937, **59**, 2207.
[17] Bardhan, Nasipuri, and Mukherjee, *J.*, 1957, 921.
[18] Woodward, Inhoffen, Larson, and Menzel, *Chem. Ber.*, 1953, **86**, 594.

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Similarly, the sodio-derivative of the β-oxo-ester (III; R = H) with 1-chloropentan-3-one [19] led successively to the dioxo-ester (III; R = CH_2·CH_2·COEt), the pentacyclic ketone (V; R = Me), and 4′-methylindeno(2′,3′:1,2)phenanthrene (VI; R = Me, R′ = R″ = H), identical with that obtained from cholic acid.[5] The ketone (V; R = Me), on condensation with methylmagnesium iodide followed by dehydration and dehydrogenation, gave the 4′,5′-dimethyl derivative (VI; R = R″ = Me, R′ = H).

To synthesise the 6′-methyl derivative (VI; R′ = Me, R = R″ = H), the methiodide of the Mannich base of butan-2-one [20] was condensed with the potassio-derivative of the β-oxo-ester (III; H), and the crude product directly hydrolysed to give a pentacyclic ketone, isolated in about 50% yield. This ketone, however, was identical with the foregoing one (V; R = Me), the identity being further established by its conversion into 4′-methyl- and 4′,5′-dimethyl-indeno(2′,3′:1,2)phenanthrene and their derivatives. This result is unexpected in view of the known [21] preponderance of 4-piperidino-3-methylbutan-2-one over the isomeric 1-piperidinopentan-3-one in the Mannich reaction product of ethyl methyl ketone. This point was not, however, pursued further at present.

Indeno(2′,3′:1,2)phenanthrene and its monomethyl and dimethyl derivatives have been characterised by their ultraviolet absorption spectra, by conversion into monoketones by chromic acid, and by formation of 2,4,7-trinitrofluorenone complexes.[22]

Experimental

M. p.s are corrected. The ultraviolet absorption spectra were recorded on a Beckman spectrophotometer.

Ethyl α-(2-1′-Naphthylethyl)-β-oxoadipate (I).—To a cold solution of potassium (4·0 g.) in t-butyl alcohol (80 ml.), ethyl β-oxoadipate (21·6 g.) was added with stirring. 2-1′-Naphthylethyl bromide (25 g.) was then added and the whole refluxed in nitrogen atmosphere for 20 hr. After removal of most of the alcohol at water-pump vacuum, the residue was acidified and extracted thoroughly with benzene. The benzene extract was washed once with water and dried (Na_2SO_4), and benzene was removed under reduced pressure. The product was distilled carefully up to 150°/0·2 mm. in order to eliminate the low-boiling impurities as far as possible and the residue (36—40 g.) used directly for the next operation.

β-(2-Carboxy-3,4-dihydro-1-phenanthryl)propionic Acid (II).—The above condensation product (40 g.) was cyclised, in 6 g. batches, by treatment with concentrated sulphuric acid (3 vols.) in a bath of carbon dioxide–acetone at −20° for 30 min., ether (1 vol.) being used as co-solvent. The brown mass was decomposed with ice and the organic matter taken up in ether. After removal of ether, the residue was hydrolysed to the acid (II) which was purified through the *diethyl ester* (12·4 g.), b. p. 210—220°/0·1 mm., the yield being 35% based on ethyl β-oxoadipate. The ester slowly solidified and crystallised from ethanol in needles, m. p. 64° (Found: C, 74·7; H, 7·0. $C_{22}H_{24}O_4$ requires C, 75·0; H, 6·8%). The corresponding acid crystallised from dilute methanol in stout prisms, m. p. 240° (Found: C, 72·6; H, 5·7. Calc. for $C_{18}H_{16}O_4$: C, 73·0; H, 5·4%). Bardhan [13a] reports m. p. 237—238°.

Methyl β-(2-Methoxycarbonyl-1-phenanthryl)propionate.—The preceding ester (6·5 g.) was heated with sulphur (0·7 g.) at 240—250° for 1 hr. and the product hydrolysed directly with 10% methanolic potassium hydroxide. The aromatic *acid*, thus obtained in about 90% yield and crystallised several times from aqueous methanol, formed thin needles, m. p. 245—247° (Found: C, 73·5; H, 5·1. $C_{18}H_{14}O_4$ requires C, 73·5; H, 4·8%). The *dimethyl ester* was prepared by boiling the acid with 5% methanolic sulphuric acid and crystallised from benzene–light petroleum (b. p. 40—60°) or methanol in light yellow flakes, m. p. 125° (Found: C, 74·4; H, 5·6. $C_{20}H_{18}O_4$ requires C, 74·5; H, 5·6%).

3′-Oxo-1,2-cyclopentenophenanthrene.—The above ester (1 g.) was heated on the water-bath with a suspension of finely divided sodium (0·1 g.) in benzene (5 ml.) containing a drop of methanol, for 2 hr. The resultant β-oxo-ester (III; R = H) was worked up as usual and on

[19] McMahon, Roper, Utermohlen, Hasek, Harris, and Brant, *J. Amer. Chem. Soc.*, 1948, **70**, 2971.
[20] Mannich and Hof, *Arch. Pharm.*, 1927, **265**, 489.
[21] Downes, Gill, and Lions, *J. Amer. Chem. Soc.*, 1950, **72**, 3464.
[22] Orchin and Woolfolk, *J. Amer. Chem. Soc.*, 1946, **68**, 1727.

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hydrolysis with boiling acetic acid and hydrochloric acid afforded 3′-oxo-1,2-cyclopentenophenanthrene (0·4 g.), plates (from benzene), m. p. 200—201° (Found: C, 87·7; H, 5·2. Calc. for $C_{17}H_{12}O$: C, 87·9; H, 5·2%). Bachmann and Kloetzel [16] report m. p. 195—196°. The analogous dihydro-compound (IV; R = H) was obtained from the ethyl ester of the acid (II) by a similar cyclisation and had m. p. 211—212°. Bardhan [13d] reports m. p. 210°.

3,4-Dihydro-8-methyl-3′-oxo-1,2-cyclopentenophenanthrene (IV; R = Me).—2-(5-Methyl-1-naphthyl)ethyl bromide was condensed with ethyl β-oxoadipate in the same way as described before, and the product (6 g.) cyclised by concentrated sulphuric acid at −20° for 20 min. to give *β-(2-carboxy-3,4-dihydro-8-methyl-1-phenanthryl)propionic acid* (2 g.), m. p. 254—256° (Found: C, 73·2; H, 5·7. $C_{19}H_{18}O_4$ requires C, 73·55; H, 5·8%). The dimethyl ester (1·7 g.), b. p. 215—220°/0·01 mm., on Dieckmann cyclisation followed by hydrolysis, as described above, afforded the ketone (0·5 g.) (IV; R = Me), thick prisms (from benzene), m. p. 250° (Found: C, 87·25; H, 6·4. Calc. for $C_{18}H_{16}O$: C, 87·1; H, 6·45%). Woodward *et al.*[18] report m. p. 237·5—241·5°.

Methyl 3′-Oxo-4′-3″-oxobutyl-1,2-cyclopentenophenanthrene-4′-carboxylate (III; R = CH_2·CH_2·COMe).—Methyl β-(2-methoxycarbonyl-1-phenanthryl)propionate, m. p. 125° (4 g.), was heated under reflux with finely divided sodium (0·33 g.) in dry thiophen-free benzene (30 ml.) and two drops of methanol until the formation of the sodio-salt of the β-oxo-ester (III; R = Na) was complete (4—5 hr.). The flask was then cooled in a freezing mixture and a solution of the methiodide of 4-piperidinobutan-2-one, prepared from the Mannich base (6 g.) and methyl iodide (6 g.), in absolute methanol (40 ml.) was gradually added with shaking. After 48 hr. at room temperature, the mixture was refluxed on the water-bath for 1 hr., cooled, and then decomposed with dilute sulphuric acid. The organic matter was taken up in benzene, the benzene layer washed successively with water, dilute alkali, and water, and the solvent evaporated. The residual *dioxo-ester* (III; R = CH_2·CH_2·COMe) crystallised from ethyl acetate (charcoal) in white plates (3·2 g., 70%), m. p. 170° (Found: C, 76·6; H, 5·65. $C_{22}H_{20}O_4$ requires C, 76·7; H, 5·6%).

5′,6′,7′,7′a-Tetrahydro-5′-oxoindeno(2′,3′:1,2)phenanthrene (V; R = H).—The preceding dioxo-ester (1·8 g.) was refluxed with acetic acid (50 ml.), concentrated hydrochloric acid (25 ml.), and water (2 ml.) for 20 hr. under carbon dioxide. On being cooled, the unsaturated *ketone* (V; R = H) was precipitated. It was filtered off and dried to give a product (1·2 g., 84%), m. p. 210—220°. This was twice crystallised from benzene, forming plates, m. p. 260—262° (Found: C, 88·8; H, 5·9. $C_{21}H_{16}O$ requires C, 88·7; H, 5·6%); $\lambda_{max.}$ (in ethanol) 219, 248, 274, 285, 299, and 329 mμ (log ε 4·38, 4·01, 4·61, 4·59, 4·62, and 4·54 respectively), $\lambda_{min.}$ 238, 250, 278, 295, and 310 mμ (log ε 3·94, 4·00, 4·52, 4·51, and 4·36 respectively).

Indeno(2′,3′:1,2)phenanthrene.—A solution of the foregoing ketone (200 mg.) in tetrahydrofuran (50 ml.) was heated under reflux with lithium aluminium hydride (200 mg.) for 2 hr. and then decomposed with cold dilute sulphuric acid. The crude alcohol (200 mg.) was heated with 30% palladium–charcoal (100 mg.) at 300—320° for 1 hr. The product was repeatedly extracted with hot benzene, and the extract filtered and reduced to small volume to afford light yellow flakes (130 mg.), m. p. 315—320°. These sublimed at 280°/0·01 mm. and finally crystallised from pyridine in colourless plates (50 mg.), m. p. 331—332° (Found: C, 94·6; H, 5·4. Calc. for $C_{21}H_{14}$: C, 94·7; H, 5·3%). The ultraviolet absorption spectrum was found identical with that recorded by Cook *et al.*[8] On oxidation with sodium dichromate in acetic acid, the hydrocarbon afforded an orange-red ketone, m. p. 208° (Found: C, 89·6; H, 4·1. Calc. for $C_{21}H_{12}O$: C, 90·0; H, 4·3%). Reported [8] m. p.s are 327—328° and 207—208°, respectively. The *2,4,7-trinitrofluorenone complex* was prepared in benzene–ethanol and obtained from benzene as a red amorphous powder, m. p. 216—217° (Found: C, 70·0; H, 3·0; N, 6·9. $C_{21}H_{14}$,$C_{13}H_5N_3O_7$ requires C, 70·2; H, 3·3; N, 7·2%).

Methyl 3′-Oxo-4′-3″-oxopentyl-1,2-cyclopentenophenanthrene-4′-carboxylate (III; R = CH_2·CH_2·COEt).—To a cold suspension of the sodio-salt of the β-oxo-ester (III; R = H) prepared from methyl β-(2-methoxycarbonyl-1-phenanthryl)propionate (3·3 g.), sodium (0·3 g.), and dry benzene (25 ml.), was added with stirring a solution of 1-chloropentan-3-one, b. p. 55—57°/18 mm. (3 g.), in benzene (10 ml.). Next day, the almost clear solution was heated under reflux for 1 hr., cooled, and decomposed with cold dilute sulphuric acid, and the product was extracted with benzene. After removal of the solvent, the residual solid crystallised from ethyl acetate to furnish the *dioxo-ester* (2·4 g.), m. p. 157° (Found: C, 77·3; H, 5·9. $C_{24}H_{22}O_4$ requires C, 77·0; H, 5·9%).

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5′,6′,7′,7′a-Tetrahydro-4′-methyl-5′-oxoindeno(2′,3′:1,2)phenanthrene (V; R = Me).—The preceding dioxo-ester (2·4 g.) was refluxed with glacial acetic acid (70 ml.), concentrated hydrochloric acid (35 ml.), and water (5 ml.) for 20 hr. under carbon dioxide. On cooling, the solution deposited the *ketone* (V; R = Me) (2·0 g.), m. p. 220—225° which was collected and crystallised from benzene in colourless plates, m. p. 252° (Found: C, 88·3; H, 6·2. $C_{22}H_{18}O$ requires C, 88·6; H, 6·0%), $\lambda_{max.}$ (in ethanol), 220, 249, 275, 286, 300, and 330 mμ (log ε 4·43, 4·08, 4·58, 4·59, 4·65, and 4·57, respectively), $\lambda_{min.}$ 238, 255, 280, 295, and 310 mμ (log ε 3·99, 4·05, 4·54, 4·54, and 4·36, respectively).

4′-Methylindeno(2′,3′:1,2)phenanthrene (VI; R = Me, R′ = R″ = H).—The ketone (V; R = Me) (300 mg.) was reduced, as above, with lithium aluminium hydride in tetrahydrofuran and the crude alcohol, m. p. 110—115°, was heated with 30% palladium–charcoal (150 mg.) at 300—320° for 1 hr. The melt was extracted repeatedly with hot benzene, and the extract filtered and evaporated. The residue sublimed at 280—290°/0·01 mm. and was finally crystallised several times from pyridine, to afford the 4′-methyl hydrocarbon (120 mg.), m. p. 274—275° (Found: C, 94·1; H, 5·8. Calc. for $C_{22}H_{16}$: C, 94·3; H, 5·7%), $\lambda_{max.}$ (in ethanol) 220, 272, 282, 298, 320, 348, 357, and 365 mμ (log ε 4·46, 4·77, 4·88, 4·56, 4·37, 3·11, 2·71, and 3·12 respectively), $\lambda_{min.}$ 246, 276, 294, 314, 344, 354, and 360 mμ (log ε 4·02, 4·76, 4·51, 4·23, 2·75, 2·65, and 2·49 respectively). The ketone derivative, obtained by oxidation of the hydrocarbon by sodium dichromate in acetic acid and purified by chromatography, afforded orange needles, m. p. 208° (Found: C, 88·65; H, 4·8. Calc. for $C_{22}H_{14}O$: C, 89·8; H, 4·8%), from ethyl acetate. Bachmann *et al.*[23] report m. p.s 275—276° and 209—210°. The *trinitrofluorenone complex* crystallised from benzene–ethanol in needles, m. p. 232° (Found: C, 70·4; H, 3·6; N, 7·35. $C_{22}H_{16}$,$C_{13}H_5N_3O_7$ requires C, 70·6; H, 3·5; N, 7·1%).

4′,5′-Dimethylindeno(2′,3′:1,2)phenanthrene (VI; R = R″ = Me, R′ = H).—The ketone (V; R = Me) (600 mg.) in dry benzene (50 ml.) was added to an excess of methylmagnesium iodide (10 mol.) in ether, and the whole was refluxed for 4 hr. and then decomposed with cold dilute sulphuric acid. The crude alcohol (700 mg.) was heated with 30% palladium–charcoal (350 mg.) at 300—320° for 1 hr. The resultant hydrocarbon was worked up in the usual way and sublimed at 290—300°/0·01 mm., to give *4′,5′-dimethylindeno(2′,3′:1,2)phenanthrene* (420 mg.), m. p. 270—275°. Two crystallisations from benzene afforded white needles, m. p. 281—282° (Found: C, 93·7; H, 6·2. $C_{23}H_{18}$ requires C, 93·9; H, 6·1%), $\lambda_{max.}$ (in ethanol) 220, 240, 273, 283, 299, 321, 350, 357, and 366 mμ (log ε 4·32, 4·06, 4·43, 4·54, 4·22, 4·07, 3·29, 2·75, and 3·01 respectively), $\lambda_{min.}$ 238, 249, 276, 294, 316, 344, 354, and 362 mμ (log ε 3·87, 3·91, 4·43, 4·19, 3·96, 2·77, 2·74, and 2·65 respectively).

The hydrocarbon (78 mg.) was oxidised by sodium dichromate (250 mg.) in hot acetic acid (5 ml.) for 5 min., affording *4′,5′-dimethyl-1′-oxoindeno(2′,3′:1,2)phenanthrene* which was collected and separated from the associated triketone by chromatography over alumina. The ketone was crystallised several times from ethyl acetate and finally obtained in orange-red needles, m. p. 255° (Found: C, 89·6; H, 5·2. $C_{23}H_{16}O$ requires C, 89·6; H, 5·2%).

The *trinitrofluorenone complex* of the hydrocarbon crystallised from benzene in red needles, m. p. 248—250° (Found: C, 71·2; H, 3·75; N, 7·0. $C_{23}H_{18}$,$C_{13}H_5N_3O_7$ requires C, 70·9; H, 3·8; N, 6·9%).

4-Piperidino-3-methylbutan-2-one.—This was prepared by the method of Mannich and Hof [20] by refluxing a mixture of piperidine hydrochloride (15 g.), paraformaldehyde (5 g.), ethyl methyl ketone (70 ml.), methanol (7·5 ml.), and concentrated hydrochloric acid (0·5 ml.) for 6 hr. The product was worked up as usual and a middle fraction (8·5 g.), b. p. 113—114°/15 mm., was used for the subsequent reaction.

Condensation of the Methiodide of the above Mannich Base with the β-Oxo-ester (III; R = H).—The ester (2·8 g.), finely divided potassium (0·4 g.), and dry thiophen-free benzene (25 ml.) were heated under reflux for 4 hr. To the potassio-derivative of the β-oxo-ester (III; R = H) thus obtained was added, with cooling, a solution of the methiodide of 4-piperidino-3-methylbutan-2-one (8·5 g.) in methanol (15 ml.). The mixture was left at room temperature for 48 hr. and then refluxed on the water-bath for 1 hr. and worked up as in the previous cases to give a highly viscous oil (3·7 g.). Without purification, this was boiled with acetic acid (100 ml.), concentrated hydrochloric acid (50 ml.), and water (2 ml.) under carbon dioxide for 20 hr. The solution was cooled to the room temperature and filtered, to afford crystals (2 g.), m. p. 220—225°. This material was purified by chromatography over alumina and

[23] Bachmann, Cook, Hewett, and Iball, *J.*, 1936, 54.

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crystallised from benzene in pale yellow flakes (1·3 g.), m. p. 250—251° (Found: C, 88·4; H, 6·1. Calc. for $C_{23}H_{18}O$: C, 88·6; H, 6·0%). The m. p. did not depress that of the ketone (V; R = Me).

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657. *The Constitution and Stereochemistry of the Lactone* $C_{10}H_{16}O_4$ *Formed in the Oxidation of Camphor by Peracids.*[1]

By J. D. CONNOLLY and K. H. OVERTON.

The minor product, $C_{10}H_{16}O_4$, of the Baeyer–Villiger oxidation of camphor is assigned the constitution and stereochemistry (II; R = R′ = OH) on degradative and spectroscopic evidence. The mechanism and stereochemistry of its formation are considered.

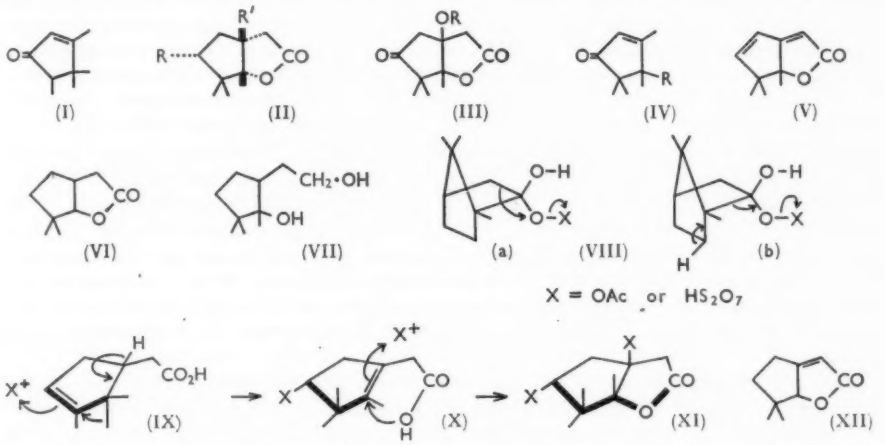
THE oxidation of camphor by peracid was first recorded [2] by Baeyer and Villiger in a paper which discloses the oxidative procedure that has become associated with their names. The principal product, α-campholide, has a structure which appears anomalous when viewed in the light of the rules subsequently formulated [3] as governing bond migration during the Baeyer–Villiger oxidation. A number of recent publications have sought to rationalise this anomaly.[4] In addition to α-campholide, Baeyer and Villiger isolated a minor product, $C_{10}H_{16}O_4$, described as lactonic. This compound is the subject of the present paper; its acid-promoted degradation to a tetramethylcyclopentenone, allegedly (I), constitutes the sole published contribution [5] to its chemistry. We have investigated the properties of this lactone and deduce for it the constitution and stereochemistry (II; R = R′ = OH) from the evidence outlined in the sequel.

The lactone was obtained either with persulphuric [2] or, more conveniently, with peracetic acid. Analysis confirmed the molecular formula assigned by Baeyer and Villiger; Kuhn–Roth oxidation demonstrated the presence of two *C*-methyl groups. The lactone consumed one equivalent of base within two minutes at 95°. The infrared spectrum had bands (in Nujol) at **1393**, **1379** (CMe_2) and (in chloroform) at **3628** (free OH), **3524** (bonded OH), and **1773** (γ-lactone) cm.$^{-1}$. Acetylation afforded either (pyridine–acetic anhydride) a monoacetate, $C_{12}H_{18}O_5$ (II; R = OAc, R′ = OH) or (refluxing acetyl chloride) a diacetate, $C_{14}H_{20}O_6$ (II; R = R′ = OAc). Oxidation with chromic acid in acetic acid smoothly furnished the cyclopentanone-lactone, $C_{10}H_{14}O_4$ (III; R = H) [$\nu_{max.}$ (in carbon tetrachloride) **1787** (γ-lactone) and **1747** (cyclopentanone) cm.$^{-1}$], which forms a monobenzylidene derivative. Thus, of the four oxygen atoms in the molecule of the original lactone, one is present as a secondary hydroxyl group, flanked by at least one methylene group and attached to a five-membered ring, the second probably as a tertiary hydroxyl, and the remaining pair in a γ-lactone system. The interrelation of these functions and definition of the framework to which they are attached followed in an unexpectedly simple manner. When the cyclopentanone (III; R = H) was refluxed with

[1] Preliminary communication: Connolly and Overton, *Proc. Chem. Soc.*, 1959, 188.
[2] Baeyer and Villiger, *Ber.*, 1899, **32**, 3625.
[3] Doering and Speers, *J. Amer. Chem. Soc.*, 1950, **72**, 5515.
[4] Murray, Johnson, Pederson, and Ott, *J. Amer. Chem. Soc.*, 1956, **78**, 981; Sauers, *ibid.*, 1959, **81**, 925; Rassat and Ourisson, *Bull. Soc. chim. France*, 1959, 1134; Meinwald and Frauenglass, *J. Amer. Chem. Soc.*, 1960, **82**, 5235.
[5] Locquin, *Compt. rend.*, 1911, **153**, 284.

0·1N-ethanolic potassium hydroxide, decarboxylation led to a hydroxycyclopentenone, $C_9H_{14}O_2$, whose spectroscopic properties indicated the structure (IV; R = OH) [$\lambda_{max.}$ 222 mμ (ε 12,000); $\nu_{max.}$ (in carbon tetrachloride) 3570 (free OH), 1710 (cyclopentenone), and 1620 (conjugated ethylenic linkage) cm.$^{-1}$]. This hydroxy-ketone (characterised as the semicarbazone) was reduced by zinc in refluxing acetic acid to the deoxy-ketone, $C_9H_{14}O$ (IV; R = H) (characterised as the 2,4-dinitrophenylhydrazone). These transformations demonstrate that the lactonic-carbonyl group is attached β (or vinylogously β) and the lactonic alkyl-oxygen atom α (or vinylogously α) with respect to the secondary hydroxyl group. Dehydration of the lactone (II; R = R′ = OH) with phosphorus oxychloride in pyridine gave the diene lactone, $C_{10}H_{12}O_2$ (V) [$\lambda_{max.}$ 262 mμ (ε 11,900); $\nu_{max.}$ (in carbon tetrachloride) 1769, 1749 (CO of lactone), and 1637 (conjugated ethylenic linkage) cm.$^{-1}$]. This, on hydrogenation over platinum, gave dihydro-β-campholenolactone [6] (VI), which was further reduced by lithium aluminium hydride to the crystalline diol [7] (VII), both of established structure. The constitution of the camphor oxidation product, $C_{10}H_{16}O_4$, as (II; R = R′ = OH) follows unambiguously from these experiments.

The tetramethylcyclopentenone obtained by the action of hot mineral acid on the dihydroxy-lactone was formulated by Locquin [5] as (I) on the basis of its degradation through a trimethyl-lævulic acid (there is no evidence for its structure) to trimethylsuccinic acid. This sequence of reactions, which we confirmed, does not, however, distinguish between the alternatives (I) and (IV; R = H) for the cyclopentenone. That the former (I) represents the correct structure follows from (*a*) non-identity with the cyclopentenone (IV; R = H) obtained as above, and (*b*) identity (established by direct



comparison of the derived semicarbazones) with the compound of structure (I) obtained by an independent route.[8]*

The formation of the dihydroxy-lactone has sound mechanistic analogy in the chemistry of camphor. Thus the transition state (VIII), instead of leading to α-campholide (*a*), can undergo the alternative collapse (*b*) to α-campholenic acid. This pathway is mechanistically akin to the Beckmann rearrangement of camphor oxime,[9] where α-campholenonitrile

* We record our gratitude to Dr. V. G. Kutcherov, Moscow, for providing an authentic specimen from the late Professor I. N. Nazarov's collection.

[6] Tiemann, *Ber.*, 1895, **28**, 2166; 1897, **30**, 405.
[7] Béhal, *Bull. Soc. chim. France*, 1904, **31**, 179.
[8] Nazarov and Bakhmutskaya, *Zhur. obshchei Khim.*, 1950, **20**, 1837.
[9] Simonsen and Owen, " The Terpenes," Cambridge Univ. Press, 1949, Vol. II, p. 437.

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is the primary product (and ring expansion to the lactam does not apparently take place). The subsequent fate of the intermediate α-campholenic acid then parallels the well-established transformation to dihydro-β-campholenolactone, with the substitution in the presence of peracid of OH^+ instead of H^+ as the cationic species at the two points indicated [(IX) ⟶ (X) ⟶ (XI)].

Support for the intermediate rôle of α-campholenic acid was found in its oxidation to the dihydroxy-lactone in improved yield under Baeyer–Villiger conditions. Further support was oxidation of dihydro-β-campholenolactone (VI) [in equilibrium with β-campholenic acid (X; X = H)] to the monohydroxy-lactone, $C_{10}H_{16}O_3$ (II; R = H, R′ = OH without stereochemical commitment) as the major product.* It had in the infrared bands (in carbon tetrachloride) at 3618 (free OH) and 1778 (γ-lactone) cm.$^{-1}$ and resisted acetylation with acetic anhydride and pyridine. Dehydration with phosphorus oxychloride in pyridine gave the oily unsaturated lactone, $C_{10}H_{14}O_2$ (XII) [$\lambda_{max.}$ 219—220 mμ (ε 11,700)], which was converted by successive reductions into the compounds (VI) and (VII).

Formation of the dihydroxy-lactone is attended by partial racemisation; this is not surprising when the proposed pathway for its genesis is taken into account, and presumably proceeds by the partly indiscriminate attack of peracid on α-campholenic acid (IX) from either side. The extent of racemisation is about the same (around 50%) whether the substrate is (+)-camphor or (+)-α-campholenic acid, provided the oxidation is carried out in a homogeneous medium (peracetic acid), but it differs unpredictably between the two substrates when persulphuric acid in a two-phase system is used. The absolute stereochemistry of the enantiomer formed in excess is assigned tentatively on the assumption that the extended Hudson lactone rule [10] can be applied to systems with an angle-methyl group: on this assumption the large positive Δ value ($[M]_D$ lactone/ethanol — $[M]_D$ lactone/N-ethanolic KOH= + 124°; see p. 3369) supports the assignment as (II).

Finally we comment on the relative stereochemistries of the three asymmetric centres in the dihydroxy-lactone. The *cis*-nature of the ring fusion is assigned on stereomechanistic grounds. Thus we believe that, to account for the steric uniformity of the product (there is no evidence, in spite of careful scrutiny, for an epimeric lactone having a *trans*-ring-fusion) and therefore the implied stereospecificity of lactonisation, this is best visualised as being concerted with, and *trans* to, peracid attack on the double bond of the intermediate (X). Such concertion is sterically favoured and mechanistically unexceptionable [11] and would necessarily result in the proposed *cis*-fusion of the two five-membered rings. The rotatory dispersion curve of the ketone (III) (see p. 3370) is in harmony with such a proposal. The relative stereochemistry of the two hydroxyl groups—there was no evidence of the diastereomeric diol—is less easily predicted and its confirmation proved difficult.

We have become aware, since our preliminary communication,[1] that the infrared evidence on which we had previously based a *cis*-assignment, might be equivocal. For a diol studied recently [12] intermolecular hydrogen bonding was shown to persist at concentrations (0·002M) below those normally regarded [13] as limiting for such bonding. While the diol (II; R = R′ = OH) still showed bonded hydroxyl absorption in 0·0003M-solution in carbon tetrachloride, this eventually disappeared on further dilution and cannot therefore result from intramolecular bonding.† It would, however, be injudicious in our view

* This compound was also obtained in minor amount when camphor or α-campholenic acid was oxidised with 5% peracetic acid.

† The absence of bonded hydroxyl absorption in the infrared solution spectrum of the monoacetate (II; R = OAc, R′ = OH) supports a *trans*-diol assignment.

[10] Klyne, *Chem. and Ind.*, 1954, 1198; Novotny, Herout, and Šorm, *Coll. Czech. Chem. Comm.*, 1960, **25**, 1500.

[11] Dauben, Hayes, Schwarz, and McFarland, *J. Amer. Chem. Soc.*, 1960, **82**, 2234 and references cited there; Woodward, Bader, Bickel, Frey, and Kierstead, *Tetrahedron*, 1958, **2**, 7.

[12] Burer and Gunthard, in "Hydrogen Bonding," Pergamon Press, London, 1959, p. 301.

[13] Cole and Jefferies, *J.*, 1956, 4391.

to infer the presence of a *trans*-diol from this observation, since the requisite data for *cis*-cyclopentane-1,3-diols are not available. It is evident that the geometry of the diol lactone is such as to favour molecular association by hydrogen bonding in very dilute solution.

Chemical evidence consistent with a *trans*-relation of the two hydroxyl groups is as follows. First, attempts to involve them in cyclic derivatives with acetone, benzaldehyde, diethyl carbonate, and oxalyl chloride under a variety of conditions (see Experimental section) were unsuccessful. Secondly, and perhaps more significantly, attempts to obtain the epimeric secondary alcohol by reducing the hydroxy-ketone (III) with sodium borohydride afforded only the known diol, apart from minor amounts of product resulting from reduction of the lactone. Such stereospecificity is explicable if reduction is supposed to occur by intramolecular hydride-transfer from an initial borate complex (as III; R = BH_3^-) of a kind discussed by Henbest and his colleagues [14] for the reduction of βγ-epoxycyclohexanols. If this were the case, the resulting diol would be *trans*-oriented.

Experimental

M. p.s were determined on the Kofler block. Infrared spectra were taken with Unicam S.P. 100 and Perkin–Elmer 13 spectrometers by Dr. G. Eglinton and his staff. Microanalyses are by Mr. J. M. L. Cameron and his staff. Chromatographic alumina was prepared and standardised according to Brockmann.[15] Light petroleum was of b. p. 60—80° unless otherwise specified.

The Dihydroxylacetone (II; R = R′ = OH).—(a) *From* (+)-*camphor*. (i) (+)-Camphor, $[\alpha]_D$ +44° (in ethanol) (75 g.), in light petroleum (120 ml.) was added during 2 hr. to potassium persulphate (600 g.) suspended in water (360 ml.) and concentrated sulphuric acid (990 ml.); the camphor solution was dropped on the disc of a vibro-mixer, placed near the surface, and the temperature was kept at 20° by cooling. Agitation was continued for a further ½ hr., and the mixture poured into ice and neutralised (pH 5) with gaseous ammonia. The resulting brown gum containing ammonium sulphate and α-campholide was removed and the aqueous filtrate continuously extracted with ether for 16 hr. The yellow, semicrystalline residue obtained on removal of ether was purified by chromatography over alumina (grade V) in 1 : 1 benzene–ethyl acetate, furnishing the *lactone* (II; R = R′ = OH) (10·0 g.) as prisms (from acetone–benzene), m. p. 192—193°, $[\alpha]_D$ +8° (*c* 0·90 in acetone), the constants not being appreciably altered by successive crystallisations (Found: C, 59·85, 60·1; H, 7·95, 8·2; *C*-Me, 14·15. $C_{10}H_{16}O_4$ requires C, 60·0; H, 8·0; 2*C*-Me, 15·0%).

Hydrolysis of the lactone (5·00 mg.) with 0·1N-sodium hydroxide (4 mol.) for 2 min. at 95° gave, on back-titration, an equivalent weight of 207 (Calc., 200).

(ii) (+)-Camphor (20 g.) in "AnalaR" acetic acid (100 ml.) was added dropwise to a stirred, cooled mixture of sulphuric acid (40 ml.) and 43% peracetic acid (40 ml.), then kept at 20° for 5 days, poured on ice, saturated with sodium chloride, and extracted with ether (3 × 150 ml.), and the combined extracts were washed with saturated sodium hydrogen carbonate and water. Chromatography of the product over alumina (grade III) afforded successively (benzene) α-campholide, (ethyl acetate–benzene; 1 : 2) non-crystalline hydroxy-lactonic material, and (ethyl acetate) dihydroxy-lactone (II; R = R′ = OH) (1·6 g.), prisms (from acetone–benzene), m. p. 180—192°, $[\alpha]_D$ +45° (in acetone), raised by two crystallisations from acetone to m. p. 192—194°, $[\alpha]_D$ +60° (*c* 1·01 in acetone). In ethanol this product had $[M]_D$ +156° (*c* 0·8) and in 1N-ethanolic potassium hydroxide $[M]_D$ +32° (*c* 0·8).

(b) *From* (+)-α-*campholenic acid*. (i) (+)-α-Campholenic acid, $[\alpha]_D$ +11° (in acetone) (11 g.), oxidised and worked up as in (a) (i), afforded the dihydroxy-lactone (3·4 g.), m. p. 190—192°, $[\alpha]_D$ +30° (in acetone). Repeated crystallisation from acetone raised these constants to m. p. 192—193°, $[\alpha]_D$ +63° (*c* 1·80 in acetone).

(ii) (+)-α-Campholenic acid (920 mg.) was oxidised as in (a) (ii), and the product chromatographed over alumina (grade V), affording dihydro-β-campholenolactone (600 mg.; eluted by benzene), monohydroxy-lactonic material (benzene–ethyl acetate; 2 : 1), and the dihydroxy-lactone (150 mg.; eluted by ethyl acetate). Crystallised twice from acetone, the last substance had m. p. 192—194°, $[\alpha]_D$ +59° (*c* 1·48 in acetone).

[14] Henbest and Nicholls, *J.*, 1957, 4608.
[15] Brockmann, *Ber.*, 1941, **74**, 73.

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Attempts to condense the hydroxy-lactone with (*a*) acetone in presence of hydrogen chloride or anhydrous copper sulphate and sulphuric acid, (*b*) diethyl carbonate or carbonyl chloride in presence of base, and (*c*) benzaldehyde in presence of acid failed, with quantitative recovery of unchanged dihydroxy-lactone.

Attempts to Form the Cyclic Oxalate (II; R + R′ = O·CO·CO·O).—(i) *With oxalyl chloride.* The dihydroxy-lactone (500 mg.) was refluxed with an excess of freshly distilled oxalyl chloride for 10 hr. The half-acid chloride (II; R = O·CO·COCl) obtained by removing unchanged oxalyl chloride *in vacuo* was hydrolysed with water, and the half-acid (II; R = O·CO·CO_2H) characterised as the *methyl ester* obtained with ethereal diazomethane; this formed needles (from acetone–benzene–hexane), m. p. 138—139° (Found: C, 54·55; H, 5·95. $C_{13}H_{18}O_7$ requires C, 54·55; H, 6·35%), $\nu_{max.}$ (in carbon tetrachloride) 3615 (free OH; no bonded OH), 1787, 1805 (shoulder) (γ-lactone), and 1753 (oxalate) cm.$^{-1}$.

The half acid (150 mg.) in dry tetrahydrofuran (10 ml.) was kept with dicyclohexylcarbodi-imide (40 mg.) for 3 days. The product, after removal of solvent, was separated into acidic [75 mg.; unchanged half-acid (infrared)] and neutral (120 mg.) fractions. The latter afforded dicyclohexylurea (insoluble in ether) (mixed m. p. and infrared spectrum) and on chromatography of the remainder (alumina; grade V) only hydroxylic fractions (infrared) but no cyclic oxalate.

The half-acid (70 mg.) and dicyclohexylcarbodi-imide (25 mg.) were kept in dry pyridine (5 ml.) for 16 hr. Dilution with ether and successive extractions with dilute hydrochloric acid and aqueous sodium hydrogen carbonate gave back unchanged acid (62 mg.).

The half-acid chloride (55 mg.) was kept in dry pyridine (7 ml.) for 1 hr. and then refluxed for 1 hr. more. Dilution with ether and working-up in the usual way gave no acidic material. The neutral fraction (40 mg.) was hydroxylic and unsaturated (infrared); chromatography did not reveal the cyclic oxalate.

(+)-*Monocamphorsulphonate* (II; R = $C_{10}H_{15}O_4S$, R′ = OH).—The dihydroxy-lactone, $[\alpha]_D$ +62° (650 mg.), and (+)-camphorsulphonyl chloride (1 mol.) were kept in pyridine for 16 hr. Chromatography of the products, obtained as usual over alumina (grade V), gave (up to 40% ethyl acetate–benzene) the (+)-*monocamphorsulphonate* (400 mg.), followed by unchanged diol (320 mg.). The ester, twice crystallised from ethyl acetate, had m. p. 181—183°, $[\alpha]_D$ +67° (*c* 0·73 in acetone) (Found: C, 58·25; H, 7·25. $C_{20}H_{30}O_7S$ requires C, 57·95; H, 7·3%).

A dihydroxy-lactone of $[\alpha]_D$ +8° gave, after six crystallisations, a (+)-camphorsulphonate, m. p. 181—183°, $[\alpha]_D$ +65° (*c* 1·4 in acetone).

Attempts to hydrolise the (+)-camphorsulphonate by oxalic acid in boiling aqueous dioxan or water were unsuccessful, affording unchanged ester and unsaturated hydroxy-lactone (infrared) respectively.

*Monotoluene-*p*-sulphonate* (II; R = $C_7H_7O_3S$, R′ = OH).—The *monotoluene-*p*-sulphonate*, obtained in the usual way and crystallised from benzene–light petroleum, had m. p. 110—112°, $\lambda_{max.}$ 226 mμ (ε 11,400) (Found: C, 57·8; H, 6·3. $C_{17}H_{22}O_6S$ requires C, 57·6; H, 6·25%).

Attempts to replace the toluene-*p*-sulphonate by acetate with inversion under a variety of conditions resulted in elimination or recovery of unchanged material.

Monoacetate (II; R = OAc, R′ = OH).—The dihydroxy-lactone (100 mg.) with pyridine and acetic anhydride at 20° afforded the monoacetate, rods (80 mg.) (from benzene), m. p. 80—82°, $[\alpha]_D$ +66° (*c* 1·92 in acetone), $\nu_{max.}$ (in carbon tetrachloride) 3615 (OH), 1784 (γ-lactone), and 1747 (acetate) cm.$^{-1}$ (Found: C, 64·1; H, 7·65. $C_{12}H_{18}O_5$,$\frac{1}{2}C_6H_6$ requires C, 64·05; H, 7·5%. Found, in material dried at 65°/2 mm.: C, 59·55; H, 7·5. $C_{12}H_{18}O_5$ requires C, 59·5; H, 7·5%).

Diacetate (II; R = R′ = OAc).—The diol, when refluxed with acetyl chloride for 2 hr., afforded the *diacetate*, plates (from ethyl acetate–light petroleum), m. p. 105—106°, $\nu_{max.}$ (in carbon tetrachloride) 1790 (γ-lactone) and 1748 (acetate) cm.$^{-1}$ (Found: C, 59·05; H, 6·8. $C_{14}H_{20}O_6$ requires C, 59·15; H, 7·1%).

Hydroxy-ketone (III; R = H).—The diol (150 mg.) in " AnalaR " acetic acid was treated with chromium trioxide (75 mg.) in 5% aqueous acetic acid at 20° for 16 hr., affording the hydroxy-ketone (III), rods (132 mg.) (from chloroform—benzene), m. p. 160—162° (Found: C, 60·85; H, 6·85. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%). A hydroxy-ketone obtained from diol of $[\alpha]_D$ +62° (in acetone) had a positive Cotton curve (*c* 0·28 in $CHCl_3$): (600 mμ) +292°; (589) +340°; (320) +2332°; (300) +1000°. The derived *acetate* obtained with refluxing acetyl chloride separated as needles from ether–hexane and had m. p. 123—125°, $\nu_{max.}$ (in

carbon tetrachloride) 1790 (γ-lactone) and 1747 (acetate and cyclopentanone) cm.$^{-1}$ (Found: C, 59·85; H, 6·5. $C_{12}H_{16}O_5$ requires C, 60·0; H, 6·7%).

The ketone (50 mg.) in 0·1N-ethanolic potassium hydroxide (10 ml.), containing freshly distilled benzaldehyde (250 mg.), was kept for 10 min. Extraction of the acidified solution with ether and removal of the aldehyde with aqueous sodium hydrogen sulphite gave, in the usual way, the *benzylidene derivative* as plates (from ethyl acetate–benzene), m. p. 150—151°, $\lambda_{max.}$ 302 mμ (ε 22,600) (Found: C, 71·2; H, 6·4. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·35%).

Reduction of the Ketone (III; R = H) *by Borohydride*.—The ketone (100 mg.) and sodium borohydride (100 mg.) were kept in methanol (10 ml., containing a few drops of water) for 3 days at 20°. The product (95 mg.) obtained with ether from the acidified reaction mixture afforded, on chromatography over alumina (grade V), the dihydroxy-lactone (II; R = R′ = OH) (80 mg.; elution by 1 : 1 benzene–ethyl acetate) and a crystalline compound, m. p. 145° (7 mg.; elution by 1 : 2 benzene–ethyl acetate) which showed no infrared carbonyl absorption and was not investigated further.

When water was used as the solvent, the more polar product was obtained in excess (5 : 2) of the diol.

Changes in the proportion of sodium borohydride and use of potassium borohydride did not afford the epimeric diol lactone.

Catalytic Reduction of the Ketone (III).—The ketone (20 mg.) and Adams catalyst (25 mg.) in ethyl acetate (4 ml.) were shaken in hydrogen until no more was absorbed (3 days; 1·2 ml., 0·58 mol.). Chromatography of the product over alumina (grade V) gave unchanged ketone (14 mg.; eluted by 9 : 1 benzene–ethyl acetate) and the dihydroxy-lactone (II; R = R′ = OH) (4 mg.; eluted by 1 : 1 benzene–ethyl acetate).

Action of Alkali on the Hydroxy-ketone (III).—The ketone (420 mg.) in dry ethanol (5 ml.) containing potassium hydroxide (3 mol.) was kept under nitrogen for ½ hr. at 80°. Potassium carbonate (190 mg.) separated during the reaction. Dilution with water and ether-extraction afforded the *cyclopentenone* (IV; R = OH), affording plates, m. p. 62—63°, from benzene–light petroleum (Found: C, 70·15; H, 8·9. $C_9H_{14}O_2$ requires C, 70·1; H, 9·15%). The *semicarbazone*, prisms from aqueous methanol, had m. p. 216—218° (decomp.), $\lambda_{max.}$ 275 mμ (ε 15,000) (Found: C, 57·0; H, 7·75; N, 19·95. $C_{10}H_{17}N_3O_2$ requires C, 56·85; H, 8·1; N, 19·9%).

Reduction of the Cyclopentenone (IV; R = OH) *with Zinc and Acetic Acid*.—The cyclopentenone (200 mg.) and zinc dust (1·5 g.) in " AnalaR " acetic acid were refluxed for 72 hr. Neutralisation with 4N-sodium hydroxide, saturation with sodium chloride, and ether-extraction furnished the deoxy-ketone (IV; R = H), b. p. 78°/10 mm., n_D^{20} 1·4730, $\lambda_{max.}$ 228 mμ (ε 12,900), $\nu_{max.}$ (film) 1697 (cyclopentenone) and 1615 (conjugated ethylenic linkage) cm.$^{-1}$. The *2,4-dinitrophenylhydrazone*, orange needles from chloroform–methanol, had m. p. 200—201°, $\lambda_{max.}$ 380 mμ (ε 27,800) (Found: C, 56·9; H, 5·5; N, 17·55. $C_{15}H_{18}N_4O_4$ requires C, 56·6; H, 5·7; N, 17·6%).

Diene Lactone (V).—The dihydroxy-lactone (750 mg.) in pyridine (20 ml.) and phosphorus oxychloride (1 ml.) (both freshly distilled) was refluxed for 2 hr. The product obtained in the usual way was eluted from alumina (grade III) by light petroleum, affording the *diene lactone* (535 mg.), b. p. 77—80°/0·7 mm., n_D^{22} 1·5129 (Found: C, 72·9; H, 7·05. $C_{10}H_{12}O_2$ requires C, 73·15; H, 7·35%).

Dihydro-β-campholenolactone and the Diol (VII).—The diene lactone (16 mg.) in ethyl acetate over platinum oxide absorbed 1·8 mol. of hydrogen in 7 hr. The product (identical by infrared spectrum with authentic dihydro-β-campholenolactone [6]) afforded, on reduction with lithium aluminium hydride, the diol (VII), plates (from benzene), m. p. 142—144°, identical with an authentic specimen [7] in m. p., mixed m. p., and infrared spectrum.

Cyclopentenone (I).—The dihydroxy-lactone (1 g.) was heated with 20% phosphoric acid (20 ml.) in a sealed tube for 6 hr. The neutral fraction of the product afforded the cyclopentenone (I), b. p. 78—80°/12 mm., n_D^{20} 1·4750, $\lambda_{max.}$ 228 mμ (ε 12,800), whose *2,4-dinitrophenylhydrazone*, orange needles (from chloroform–methanol), had m. p. 202—203° [mixed m. p. with the 2,4-dinitrophenylhydrazone of (IV; R = H) 184—188°], $\lambda_{max.}$ 385 mμ (ε 24,800) (Found: C, 56·45; H, 5·95; N, 17·55. $C_{15}H_{18}N_4O_4$ requires C, 56·6; H, 5·7; N, 17·6%). The semicarbazone, m. p. 176—178°, was identical in m. p., mixed m. p., and infrared spectrum with an authentic specimen.[6]

αββ-*Trimethyl-lævulic Acid Semicarbazone*.—The cyclopentenone (I) in dry methylene chloride (20 ml.) was treated at −70° with ozonised oxygen, until the absorption maximum at

228 mμ had disappeared (½ hr.). Decomposition of the ozonide with water (10 ml.) at 95° and ether-extraction afforded trimethyl-lævulic acid (426 mg.) as a yellow oil, whose *semicarbazone* formed plates, m. p. 175—177°, from aqueous methanol (Found: C, 50·5; H, 8·1; N, 19·4. $C_9H_{17}N_3O_3$ requires C, 50·2; H, 7·95; N, 19·5%).

Trimethylsuccinanil.—The trimethyl-lævulic acid (100 mg.) was added to bromine (350 mg.) and sodium hydroxide (225 mg.) in water (4 ml.). The solution was kept for 10 min., reduced to 1 ml. at the water-pump, and acidified with hydrochloric acid. The crude trimethylsuccinic acid obtained with ether (60 mg.; m. p. 144—154°) was refluxed with aniline (300 mg.) for ½ hr. The product, worked up as usual, afforded from aqueous ethanol needles of *trimethylsuccinanil*, m. p. 131—132° after sublimation (Found: C, 72·2; H, 7·05; N, 6·75. $C_{13}H_{15}NO_2$ requires C, 71·85; H, 6·95; N, 6·45%).

The Hydroxy-lactone (II; R = H, R′ = OH).—Dihydro-β-campholenolactone [6] (1·6 g.) was oxidised by the procedure (a) (i) used for (+)-camphor. Chromatography of the product over alumina (grade V) afforded unchanged dihydro-β-campholenolactone (1·4 g.; eluted by benzene) and the *hydroxy-lactone* [80 mg.; eluted by ethyl acetate–benzene; 1 : 9)], rods (from benzene–light petroleum), m. p. 143—145° (sublimed at 90°/0·5 mm.) (Found: C, 65·2; H, 8·8. $C_{10}H_{16}O_3$ requires C, 65·2; H, 8·75%).

The hydroxy-lactone was unchanged when treated with acetic anhydride–pyridine at 20°.

The hydroxy-lactone (250 mg.) was dehydrated with phosphorus oxychloride in pyridine, and the product, dissolved in light petroleum, filtered through alumina, affording the unsaturated *lactone* (XII) (176 mg.), b. p. 88°/0·8 mm., $\lambda_{max.}$ 219 mμ (ε 11,700). (Found: C, 71·75; H, 8·25. $C_{10}H_{14}O_2$ requires C, 72·25; H, 8·5%).

Hydrogenation over platinum oxide in ethyl acetate gave dihydro-β-campholenolactone, which was converted into the diol (VII), identical with material obtained from the diene lactone (V).

We are grateful to Professor D. H. R. Barton, F.R.S., for his critical interest and Professors G. Ourisson and W. Klyne for rotatory dispersion measurements. One of us (J. D. C.) is indebted to the D.S.I.R. for a maintenance grant.

Chemistry Department, The University, Glasgow. [*Received, February 10th*, 1961.]

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658. *Infrared Spectra of Substituted Salicylaldehydes.*

By C. J. W. Brooks and J. F. Morman.

Infrared data are reported for a group of substituted salicylaldehydes and some related compounds with particular reference to nitro-derivatives. The character of the hydroxyl, carbonyl, and nitro-absorptions of 3-nitrosalicylaldehyde (in chloroform or carbon tetrachloride) indicates that the phenolic group is hydrogen-bonded chiefly to the nitro-group, whereas in 2-hydroxy-3-nitroacetophenone and methyl 3-nitrosalicylate the chelated *o*-hydroxy-carbonyl species predominate. The effects of acetonitrile and pyridine on the hydrogen-bond equilibria are discussed.

After the early spectroscopic investigations of hydrogen bonding in salicylaldehyde [1] many studies have been made of the infrared absorption of this compound, which exhibits a diffuse hydroxyl band [2] near 3150 cm.$^{-1}$ and a sharp carbonyl band at 1669 cm.$^{-1}$ (in carbon tetrachloride).[3] As with other *ortho*-hydroxycarbonyl compounds, the stability of the hydrogen bond renders the absorption somewhat insensitive to the physical state of the compound: thus the salicylaldehyde carbonyl band is reported as virtually the same in chloroform, acetonitrile, and butan-1-ol solutions.[4] However, for pyridine or

[1] Errera and Mollet, *J. Phys. Radium*, 1935, **6**, 281.
[2] Errera and Sack, *Trans. Faraday Soc.*, 1938, **34**, 728; Martin, *Nature*, 1950, **166**, 474.
[3] Hunsberger, *J. Amer. Chem. Soc.*, 1950, **72**, 5626.
[4] Yamada, *Bull. Chem. Soc. Japan*, 1959, **32**, 1051.

trimethylamine solutions a band is observed near 1680 cm.$^{-1}$ and is regarded [5] as a " free " carbonyl band, the phenolic group being hydrogen-bonded to the basic solvent. In this paper we report studies on a number of substituted salicylaldehydes and related compounds in several solvents with reference to the effects of alkyl and nitro-substituents. Particular attention has been given to 3-nitrosalicylaldehyde and its analogues, in which alternative hydrogen bonds may be formed. The possibility of competitive intramolecular hydrogen bonding in aromatic systems was adumbrated by Hoyer,[6] and Baker and Kaeding [7] recently provided a spectroscopic demonstration of coexisting alternative hydrogen-bonded forms of 2,6-unsymmetrically disubstituted phenols. Since the completion of our experiments, Hoyer and Hensel [8] have presented evidence for this type of rotational isomerism in 3,5-dinitrosalicylaldehyde.

Experimental

Materials.—Most of the substituted salicylaldehydes were kindly supplied by Professor M. Crawford and Mr. J. W. Rasburn.[9] 3-Nitro-, 5-nitro-, and 3,5-dinitro-salicylaldehyde,[10] 5-nitro-β-resorcylaldehyde,[11] 2-hydroxy-3-nitro-,[12] 2-hydroxy-5-nitro-,[12] 2-hydroxy-4-methyl-,[13] and 2-hydroxy-4,6-dimethylacetophenone [14] were prepared essentially by the methods cited. Methyl esters were prepared with diazomethane. All samples were finally purified by sublimation or short-path distillation at 0·1 mm. Purity of liquid samples was checked by gas–liquid chromatography: a minor impurity was detected in the sample of *o*-fluorobenzaldehyde. Pyridine for spectroscopic measurements was redistilled twice from potassium hydroxide immediately before use: other solvents were purified as described previously.[15]

Measurements.—Most of the results shown in Table 1 were determined with a Unicam S.P.100 spectrophotometer operated under dry-air conditions as described elsewhere: [15] the remainder of the work was carried out with a Mark II version of this instrument used under a vacuum. Water vapour was used for calibration in the 1300—1750 and 3500—3650 cm.$^{-1}$ regions, and methane in the 2700—2900 cm.$^{-1}$ region.[16] The computed theoretical spectral slit widths (for the Mark II instrument) were 6, 4, 4, and 5 cm.$^{-1}$, at 3500, 1650, 1350, and 650 cm.$^{-1}$, respectively. Apparent extinction coefficients (ε_a) are expressed as l. mole^{-1} cm.$^{-1}$. Spectra recorded from 650 to 3650 cm.$^{-1}$ of substituted salicylaldehydes as Nujol mulls or liquid films will appear in the D.M.S. Index (Butterworths) as spectral cards Nos. 7583—7599.

Results and Discussion

1600—3650 cm.$^{-1}$ *Region.*—Data for the hydroxyl, aldehyde C–H, and carbonyl absorptions of a group of substituted salicylaldehydes and some related compounds are recorded in Table 1. The carbonyl bands are close to the region of " aromatic " absorption and the possibility of vibrational resonance with combination bands has been invoked [5] to account for the strong band near 1650 cm.$^{-1}$ in salicylaldehyde (cf. Fig. 1). However, the most intense bands in the 1600—1700 cm.$^{-1}$ region are regarded as carbonyl group vibrations since they occur at the expected frequencies and undergo normal solvent shifts. The designation of the 1634 cm.$^{-1}$ band of β-resorcylaldehyde (No. 7) as a carbonyl vibration [17] seems in error. Alkyl substituents increase the band width but the integrated

[5] Chiorboli and Mirone, *Ann. Chim.* (*Italy*), 1958, **48**, 363.
[6] Hoyer, *Z. Elektrochem.*, 1956, **60**, 381; 1957, **61**, 313; *Chem. Ber.*, 1956, **89**, 146.
[7] Baker and Kaeding, *J. Amer. Chem. Soc.*, 1959, **81**, 5904.
[8] Hoyer and Hensel, *Z. Elektrochem.*, 1960, **64**, 958.
[9] Crawford and Rasburn, *J.*, 1956, 2155.
[10] von Miller, *Ber.*, 1887, **20**, 1927; Lovett and Roberts, *J.*, 1928, 1975.
[11] Gattermann, *Annalen*, 1907, **357**, 313.
[12] Lindemann and Romanoff, *J. prakt. Chem.*, 1929, **122**, 214.
[13] Rosenmund and Schnurr, *Annalen*, 1928, **460**, 56.
[14] Smith and Opie, *J. Org. Chem.*, 1941, **6**, 427.
[15] Brooks, Eglinton, and Morman, *J.*, 1961, (*a*) 106; (*b*) 661.
[16] Downie, Magoon, Purcell, and Crawford, *J. Opt. Soc. Amer.*, 1953, **43**, 941.
[17] Pinchas, *Analyt. Chem.*, 1957, **29**, 334.

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intensities are not strikingly altered; the value for salicylaldehyde agrees with that given by Yamada [4] ($A = 2{\cdot}6 \times 10^4$ l. mole^{-1} cm.$^{-2}$ in carbon tetrachloride or chloroform; cf. also Krueger and Thompson [18]). The marked lowering of the carbonyl frequency in 6-methyl-3-t-butylsalicylaldehyde (No. 5) and in 2-hydroxy-4,6-dimethylacetophenone (No. 22) parallels the effects attributed to steric compression in the salicylic acid series.[15b]

The 5-nitroaldehydes (Nos. 8, 9, and 11) show carbonyl bands similar to those of their parent compounds (Nos. 1, 3, and 5), but the spectra of the 3-nitro-derivatives are strikingly different (Fig. 1); in every example the principal band in the carbonyl region occurs near 1700 cm.$^{-1}$ with minor variations depending on the substituent at the 5-position. A second, smaller band is noted near 1670 cm.$^{-1}$. The relative optical density

TABLE 1. *Hydroxyl, aldehyde* C–H *and carbonyl absorptions of substituted salicylaldehydes and related compounds.*

No.	Compound Substituents	Carbon tetrachloride ν_{OH} [b]	ν_{CH}		ν_{CO}	$\Delta\nu_{\frac{1}{2}}$ [a]	ε_a	Chloroform ν_{CO}	$\Delta\nu_{\frac{1}{2}}$ [a]	ε_a
Salicylaldehydes [j]										
1	None	(3150)	2840	2749	1669	7	1030	1666	9	840
2	5-Bu^t	(3180)	2831	2740	1663	14	830	1656	18	675
3	3-Pr^i	(3130)	2840	2747	1661 ‡	(25)	460	1653	(33)	465
4	3,5-Bu$^t_2$	(3100)	2839	2742	1654	14	625	1648	19	655
5	3-Bu^t, 6-Me	(3000)	weak	weak	1641	17	550	1635 [c]	24	490
6	3-OMe [d]	(3150)	2841 [e]	2745	1661	13	665	1659	17	580
					1678sh	*	<170	1676	15 †	180
					1695	*	<55			
7	4-OH [f]	(3060)	2835	2747	1660	10	975	1657	15	745
8	5-NO_2	(3095)	2861	2734	1674	8	1045	1670	13	895
9	3-Pr^i, 5-NO_2	(3100)	2851	2737	1668	14	645	1665	16	565
10	3-Ph, 5-NO_2	3065	2852	2738	1666	11	665	1663	15	625
11	3-Bu^t, 5-NO_2, 6-Me	(2950)	2876	—	1646	15	580	1643	18	550
12	3-NO_2	3170	2876	2770	1701	8	620	1694	13	455
					1676	14	110	1673	17	185
13	3,5-$(NO_2)_2$	(3140)	2881	2773	1707	7	615	1702	10	440
					1680	11	205	1677	13 †	250
								1653	16 †	250
14	3-NO_2, 5-Bu^t	3195	2874	2766	1700	6	810	1694	12	495
					1674	13	110	1670	*	215
15	3-NO_2, 5-Cl	3200	2878	2766	1702	7	685	1697	11	510
					1678	10	110	1675	12	175
16	3-NO_2, 5-OMe	3220	2878 [g]	2766	1700	11	525	1694	14	480
					1679	*	55	1676	*	110
17	3-NO_2, 5-Ph	3185	2875	2765	1700	8	665	1694	14	455
					1675	12	125	1671	15	220
18	4-OH, 5-NO_2	3160	2845	(2730)	1674	(10)	785	1674	11	650
				(2760)	1665	(10)	1035	1663	*	1090
2-Hydroxyacetophenones [k]										
19	None	(3025)	—	—	1646	12	655	1642	17	620
20	3-Me	(3000)	—	—	1641	12	540	1638	16 †	445
								(1630sh)	*	*
21	4-Me	(2960)	—	—	1640	(22)	515	1637	21 †	590
					(1627sh)	*	<290	(1624sh)	*	*
22	4,6-Me_2	(2950)	—	—	1629	*	(450)	1628	17 †	540
								(1610sh)	*	*
23	5-NO_2	(3000)	—	—	1657	18	555	1653	21	520
24	3-NO_2	(3100)	—	—	1693	12	250	1684	23 †	115
					1658	13	310	1656	17	390
Methyl salicylates										
25	5-NO_2	(3140)	—	—	1690	13	680	1687	18	570
26	3-NO_2	(3100)	—	—	1690	13	575	1688	16	525
					1722	*	<60			
					1746	*	60			
27	3,5-$(NO_2)_2$	(3000)	—	—	1695	12	675	1695	14	680
					1727	*	*			
					1751	*	50			

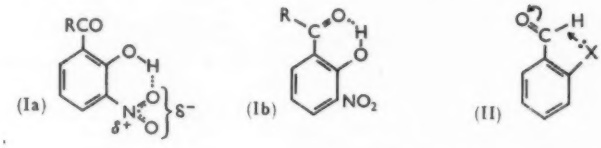
[18] Krueger and Thompson, *Proc. Roy. Soc.*, 1959, *A*, **250**, 22.

TABLE 1. (*Continued.*)

No.	Compound Substituents	Carbon tetrachloride ν_{OH} [b]	ν_{CH}		ν_{CO}	$\Delta\nu_{\frac{1}{2}}$ [d]	ε_a	Chloroform ν_{CO}	$\Delta\nu_{\frac{1}{2}}$ [d]	ε_a
Benzaldehydes [m]										
28	*o*-OMe	—	2862	2759	1695	7	735	1688	14	510
					1666 [n]	*	60	1665 [n]	13 †	170
29	*o*-F	—	2860	2762	1703	7	685	1698	13	*
					(1684sh)	*	<70	1683	8 †	*
30	*o*-NO_2	—	2869	2766	1706	10	520	1702	14	450
			2890							
31	*m*-OMe	—	2834	2726	1709	10	640	1702	15	505
					1686 [n]	11 †	105	1684 [n]	12	225
32	*m*-Cl	—	2827	2724	1709	9	730	1703	12	910
33	*m*-NO_2	—	2833	2730	1713	11	530	1708	12	615
			2809		1727 [n]	9	175	1727 [n]	10 †	105
34	2,3-$(OMe)_2$	—	2858	2745	1696	9	620	1690	18	410
35	3,4-$(OMe)_2$	—	2839	2754	1701	11 †	410	1698	14 †	290
			2812	2721	1687	10 †	460	1682	16	565

Values in parentheses are approximate. — No band present. * Not measured. † Estimated by band reflection. ‡ Unsymmetrical band. [b] The approximate band centre is cited. [c] Fused to aromatic band at 1616 $cm.^{-1}$. [d] The carbonyl nature of the bands cited is discussed in the text. [e] Superimposed aldehyde and methoxyl bands. [f] Free OH band at 3593 $cm.^{-1}$. [g] A band at 2839 $cm.^{-1}$ is ascribed to methoxyl (ref. *h*). [h] Henbest, Meakins, Nicholls, and Wagland, *J.*, 1957, 1462. [i] A strong band at 3095 $cm.^{-1}$ is ascribed to $2\nu_{NO_2}$ (asym.). [j] 0·0017M in CCl_4, *ca.* 0·02—0·06M in $CHCl_3$. [k] 0·0015M in CCl_4, *ca.* 0·02—0·06M in $CHCl_3$. [l] 0·00135M in CCl_4, *ca.* 0·045M in $CHCl_3$. [m] 0·0017M in CCl_4, *ca.* 0·05—0·08M in $CHCl_3$. [n] Not regarded as carbonyl bands (see text).

is unaltered by dilution from 0·06M to 0·0017M in carbon tetrachloride but is affected by the solvent (see below). The major band frequency is indicative of an aromatic aldehyde group not involved in a hydrogen bond, and the minor band is at a typical salicylaldehyde frequency. These absorptions are ascribed to the species (Ia; R = H) and (Ib; R = H)



respectively (cf. ref. 8): this assignment is further discussed below. The first overtones of the principal carbonyl bands in 3- and 5-nitrosalicylaldehydes are unusually prominent (Fig. 1) and their positions support the assignments made. The effects of nitro-substituents on the carbonyl absorptions of 2-hydroxyacetophenone and methyl salicylate (Fig. 1) are in harmony with these views. The 5-nitro-derivatives both show single bands. In the spectrum of 2-hydroxy-3-nitroacetophenone two bands are observed, at the frequencies expected for (Ia; R = Me) and (Ib; R = Me), with the latter predominating. Methyl 3-nitrosalicylate exhibits only low absorption in the region expected for form (Ia; R = OMe): the bands at 1722 and 1746 $cm.^{-1}$ probably correspond to two conformations of the methoxycarbonyl group in (Ia; R = OMe).[15a] The principal band, ascribed to (Ib; R = OMe), closely resembles that of the 5-nitro-isomer. Entirely analogous behaviour is shown by methyl 3,5-dinitrosalicylate.

3-Methoxysalicylaldehyde (No. 6) shows complex absorption in the carbonyl region. The more intense bands near 1660 and 1676 $cm.^{-1}$ are presumed to arise from the chelated carbonyl group, while the band near 1695 $cm.^{-1}$ might be interpreted as due to a species analogous to (Ia). The present data do not allow firm assignments to be made.

Comment is necessary on two features of the data for substituted benzaldehydes (Table 1, Nos. 28—35). The carbonyl frequency (benzaldehyde, 1709 $cm.^{-1}$ in CCl_4) is lowered by *ortho*-substitution even by the strongly electron-attracting nitro-group. This

is assumed to result from enhanced polarisation of the carbonyl group in the favoured conformation (II) since the frequency shifts are similar to those ascribed to the corresponding species in *ortho*-substituted methyl benzoates.[15a] The occurrence of two bands

FIG. 1.

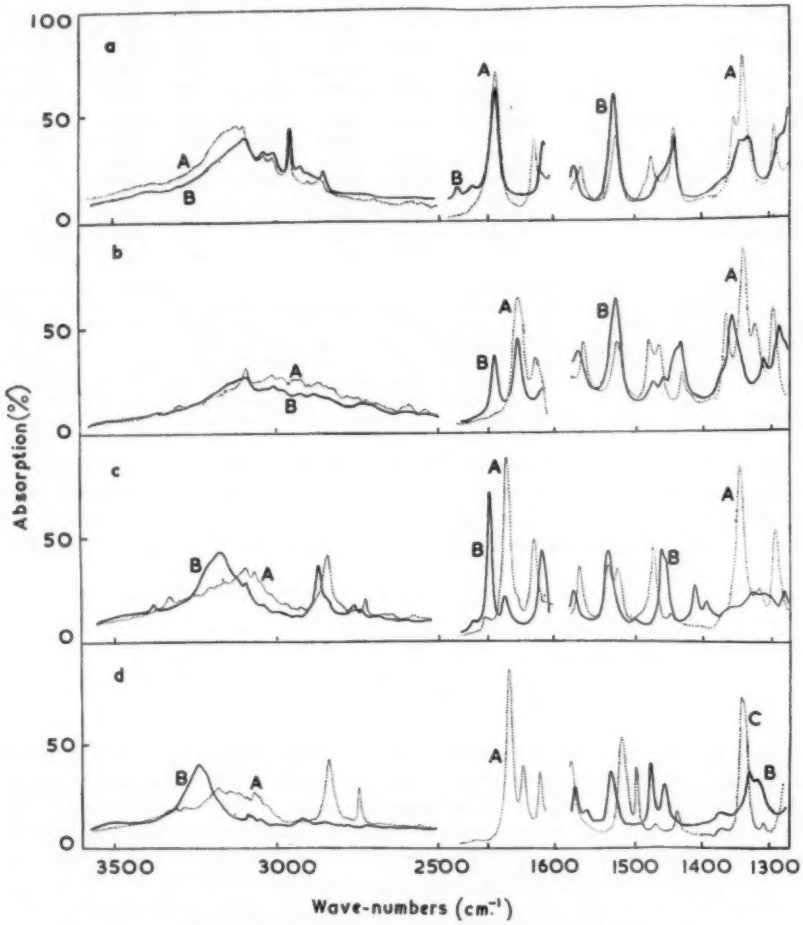


FIG. 1a. A, *Methyl 5-nitrosalicylate*; B, *methyl 3-nitrosalicylate.*
FIG. 1b. A, *2-Hydroxy-5-nitroacetophenone*; B, *2-hydroxy-3-nitroacetophenone.*
FIG. 1c. A, *5-Nitrosalicylaldehyde*; B, *3-nitrosalicylaldehyde.*
FIG. 1d. A, *Salicylaldehyde*; B, o-*nitrophenol*; C, p-*nitrophenol.*

Concentrations as noted in Tables 1 *and* 2: CCl_4 *solutions*, 20 mm. *cells* (3650—2500 cm.$^{-1}$), 5 mm. *cells* (1750—1600 cm.$^{-1}$). $CHCl_3$ *solutions*, 0·11 mm. *cells* (1600—1250 cm.$^{-1}$).

in the carbonyl region of the spectra of *o*- and *m*-methoxybenzaldehyde, *m*-nitrobenzaldehyde, and 3,4-dimethoxybenzaldehyde is also notable. In the first three cases the relatively unperturbed carbonyl band is identifiable by its intensity and position, and by typical solvent shifts: the minor band frequency is solvent-insensitive, but the band intensity falls with increasing separation between this absorption and the carbonyl band. It thus appears probable that these subsidiary bands are combination modes strengthened

by resonance with the carbonyl vibrations. The absorption of 3,4-dimethoxybenzaldehyde is regarded as a more extreme example of this effect in which the carbonyl vibration mode contributes to both the observed bands.

In the hydroxyl region, 3-nitrosalicylaldehyde and its derivatives show a single broad band near 3200 cm.$^{-1}$, similar to that of *o*-nitrophenol and distinct from the weaker, diffuse bands near 3150 cm.$^{-1}$ typical of salicylaldehyde (cf. Fig. 1).

The 3-nitrosalicylaldehyde structure is further distinguished by the band attributed to aldehyde C–H stretching which occurs near 2765 cm.$^{-1}$, as compared with the " normal " value near 2740 cm.$^{-1}$. The second band generally associated with benzaldehydes, regarded by Pinchas [17] as a combination band of the C_{CHO}–H in-plane bending vibration near 1380 cm.$^{-1}$ with a ring vibration near 1470 cm.$^{-1}$, occurs near 2875 cm.$^{-1}$ in 3-nitrosalicylaldehyde and its nuclear-substituted derivatives: in the remaining compounds it appears to be near 2840 cm.$^{-1}$ but the assignment is uncertain in aldehydes having alkyl

TABLE 2. *Nitro-group absorptions of nitrosalicylaldehydes and related compounds (ca. 0·02—0·06M in $CHCl_3$).*

Compound No.	Substituents	$\nu_{(asym.)}$	$\Delta\nu_{\frac{1}{2}}$ *	ε *	$\nu_{(sym.)}$	$\Delta\nu_{\frac{1}{2}}$ *	ε *
Salicylaldehydes							
8	5-NO_2	1541	13	245	1347	9	1120
		1526	13	230			
9	3-Pr^i, 5-NO_2	1532	21	385	1352	12	675
					1320	14	695
10	3-Ph, 5-NO_2	1539	20	310	1346	11	730
11	3-Bu^t, 5-NO_2, 6-Me	1523	23	335	1342	*	430
12	3-NO_2	1537	16	280	1350	*	100
					1331	*	100
13	3,5-$(NO_2)_2$	(1554)	*	325	1349	12	1045
14	3-NO_2, 5-Bu^t	1538	18	415	1369	*	(200)
					1325	*	(200)
15	3-NO_2, 5-Cl	1538	19	350	1352	*	<130
					1312	*	185
16	3-NO_2, 5-OMe	1541	14	720	1321	18	390
17	3-NO_2, 5-Ph	1542	15	470	1332	*	<200
					1312	*	<200
18	4-OH, 5-NO_2	1538	18	500	1347 ‡	*	285
2-Hydroxyacetophenones							
23	5-NO_2	1531	18	235	1345	10	985
24	3-NO_2	1532	17	465	1362	21	360
Methyl salicylates							
25	5-NO_2	1530	16	365	1344	10	1130
					1357	12 †	485
26	3-NO_2	1533	12	700	1347	*	<360
					1334	*	<360
Miscellaneous compounds							
36	*o*-Nitrophenol	1540	14	300	1334	12 †	330
					1321	*	265
37	*m*-Nitrophenol	1532	11	1090	1357	9	705
38	*p*-Nitrophenol	1522	12	595	1346	13	1080
39	*o*-Nitroanisole	1527	14	695	1356	19	300
30	*o*-Nitrobenzaldehyde	1532	12	685	1349	10	440
33	*m*-Nitrobenzaldehyde	1539	9	615	1345	7	700

For symbols see Table 1.

C–H bands near 2875 cm.$^{-1}$. Elevation of both " aldehyde " C–H frequencies has been noted [17,19] in 2,3- and 2,6-disubstituted benzaldehydes and attributed to steric effects,[19] though in all the examples, except 2,6-dimethylbenzaldehyde,[19] the effect could be associated with strong dipole interactions, as proposed by Schneider and Bernstein [20] to

[19] West and Whatley, *Chem. and Ind.*, 1959, **333.**
[20] Schneider and Bernstein, *Trans. Faraday Soc.*, 1956, **52**, 13.

account for the raised C–H frequency in solid aldehydes as compared with solutions. Evidently the normal values for 3-alkylsalicylaldehydes (Nos. 3, 4) reflect the stabilisation of the aldehyde C–H environment by the hydrogen bond.

1250—1600 cm.$^{-1}$ *Region.*—The effects of hydrogen bonding on nitro-group vibrations are not well established. One difficulty lies in the complex nature of these vibrations: another is that the regions of absorption concerned are populated by many other strong bands, particularly in aromatic compounds. Even in the nitro-alcohols Urbański's [21] report that the symmetric stretching vibration occurs at 1310 cm.$^{-1}$ in the hydrogen-bonded compounds is confused by the absorption at this frequency due to the alcohol group itself. For *o*-nitrophenol (and *o*-nitroanisole) the reported [22,23] asymmetric stretching frequency (*ca.* 1530 cm.$^{-1}$) is little different from that of nitrobenzene, whereas for *o*-nitroaniline, in which there appears to be no hydrogen bond,[24] an appreciably lower value (1511 cm.$^{-1}$ in $CHBr_3$) has been recorded.[22] In view of the lack of quantitative data for *o*-nitrophenols, the substituted 3-nitrosalicylaldehydes and other relevant compounds have now been examined. The absorption due to nitro-groups was investigated with 0·11 mm. cells to allow adequate transmission over the range 1250—1750 cm.$^{-1}$. Full results were obtained for chloroform solutions (Table 2): where solubility permitted, spectra were determined also for carbon tetrachloride solutions, and no major differences were noted. In the 5-nitro-aldehydes the asymmetric and symmetric nitro-vibrations give rise to sharp, intense bands near 1540 and 1340 cm.$^{-1}$ respectively: only in the 3-isopropyl derivative (No. 9) is there some ambiguity in the latter assignment, as two equally intense bands occur at 1352 and 1320 cm.$^{-1}$. The 3-nitro-aldehydes also exhibit a band near 1540 cm.$^{-1}$ but in the region of the symmetric vibration they are profoundly different: no notably intense band is present, and apart from a general increase in "background" absorption the spectra in the 1300—1400 cm.$^{-1}$ region resemble those of the aldehydes lacking nitro-substituents. The virtual submergence of the symmetric vibration cannot be ascribed purely to hydrogen-bond formation since in spectra of 5-nitro-β-resorcylaldehyde (No. 18) and of *o*-nitrophenol (No. 36) bands attributable to this mode are quite prominent. The effects evidently result from the buttressing inherent in 1,2,3-trisubstitution: thus, from results reported by Dearden and Forbes,[23] the symmetric bands shown by *o*-nitrophenols bearing alkyl substituents in the 3- and/or 6-positions are weaker than those of *o*-nitrophenol and 4,5-dimethyl-2-nitrophenol. (Frequency shifts of the type noted by van Veen, Verkade, and Wepster [25] for 2,3-disubstituted nitrobenzenes are not discernible in our work.) It is concluded that the results are consonant with strong hydrogen bonding between the nitro- and the phenol group in 3-nitrosalicylaldehyde and its congeners. In 2-hydroxy-3-nitroacetophenone and methyl 3-nitrosalicylate, symmetric nitro-bands are observed which are comparable in frequency, intensity, and breadth with those of *ortho*-substituted nitro-compounds lacking hydrogen bonds, *e.g.*, *o*-nitrobenzaldehyde (No. 30) and *o*-nitroanisole (No. 39).

Solvent Studies.—In order to confirm that the results so far described could be correctly construed in terms of equilibria between the hydrogen-bonded species (Ia) and (Ib), the effects of (i) a more polar solvent (acetonitrile) and (ii) a basic solvent (pyridine) were explored. Results for acetonitrile solutions are presented in Table 3. The two carbonyl bands observed in the 3-nitro-derivatives undergo solvent shifts comparable, respectively, with those of typical chelated and unchelated carbonyl groups. The effect on the relative intensity of the bands is significant (cf. Fig. 2). For 3-nitrosalicylaldehyde the ratios of the intensities (ε_a) of the high- and low-frequency bands in CCl_4, $CHCl_3$, and MeCN are respectively 5·6, 2·4, and 1·4: for 2-hydroxy-3-nitroacetophenone, 0·8, 0·3, and *ca.* 0·15.

[21] Urbański, *Roczniki Chem.*, 1957, **31**, 53.
[22] Franck, Hörmann, and Scheibe, *Chem. Ber.*, 1957, **90**, 330.
[23] Dearden and Forbes, *Canad. J. Chem.*, 1960, **38**, 1852.
[24] Urbański and Dabrowska, *Chem. and Ind.*, 1958, 1206; Dyall and Hambly, *ibid.*, p. 262.
[25] van Veen, Verkade, and Wepster, *Rec. Trav. chim.*, 1957, **76**, 801.

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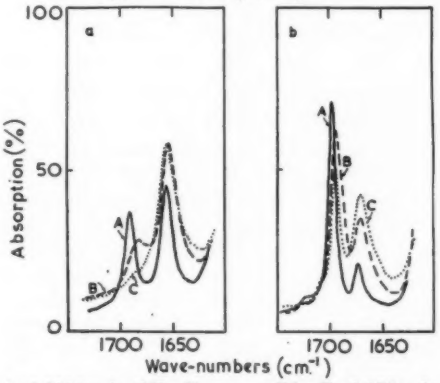
TABLE 3. *Carbonyl absorptions* (CH_3·CN *solutions, ca.* 0·015M).

	Compound	ν_{CO}	$\Delta\nu_{\frac{1}{2}}$ [a]	ε [a]		Compound	ν_{CO}	$\Delta\nu_{\frac{1}{2}}$ [a]	ε [a]
1	Salicylaldehyde	1666	9	780	24	2-Hydroxy-3-nitro-	1657	20	445
		1646 [a]	13	315		acetophenone	(1685)	*	<70
33	*m*-Nitrobenzaldehyde	1707	8	765	28	*o*-Methoxybenzaldehyde	1690	10	690
		1727	*	85			1666 [a]	*	125
8	5-Nitrosalicylaldehyde	1669	14	715	30	*o*-Nitrobenzaldehyde	1703	13	465
		1691	*	<65	31	*m*-Methoxybenzaldehyde	1704	10	660
		1706	*	<65			1685 [a]	12 †	175
12	3-Nitrosalicylaldehyde	1696	9	390	6	3-Methoxysalicylalde-	1658 ‡	20	495
		1672	22	295		hyde	1675	*	180
19	*o*-Hydroxyacetophenone	1645	16	570			1689	11 †	135
23	2-Hydroxy-5-nitroaceto- phenone	1654	20	555					

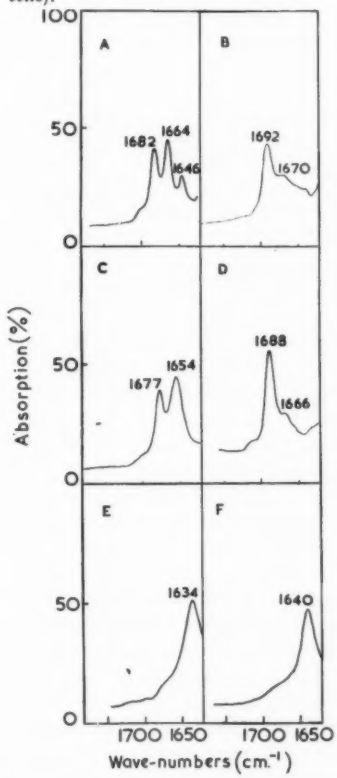
For symbols see Table 1. [a] Not regarded as a carbonyl band.

FIG. 2. (a) *2-Hydroxy-3-nitroacetophenone* (b) *3-Nitrosalicylaldehyde.*



A, 0·0015M *in* CCl_4 (5 mm. *cells*); B, 0·075M *in* $CHCl_3$ (0·11 mm. *cells*); C, 0·015M *in* Me·CN (0·5 mm. *cells*).

FIG. 3. A, *Salicylaldehyde*; B, *3-nitrosalicylaldehyde*; C, *5-t-butylsalicylaldehyde*; D, *5-nitrosalicylaldehyde*; E, *6-methyl-3-t-butylsalicylaldehyde*; F, *6-methyl-5-nitro-3-t-butylsalicylaldehyde. Pyridine solutions*, 0·05M (0·11 mm. *cells*).



These results support the view that the observed bands correspond to species (Ia) and (Ib), *i.e.*, the form with the unchelated nitro-group is relatively stabilised by increasing the solvent polarity. From the data of Eda and Ito [26] it may be computed that the dipole

[26] Eda and Ito, *Bull. Chem. Soc. Japan*, 1956, **29**, 524; 1957, **30**, 164.

moment of (Ib) should exceed that of (Ia). Similar intensity effects have been discussed [15a] for other examples of conformational isomerism.

The effects of pyridine on the absorption of *ortho*-hydroxycarbonyl compounds may be expected to be derived chiefly from its bonding to the phenolic hydrogen atom. Carbonyl and nitro-absorption data are recorded in Table 4. The nitro-absorptions are closely similar to those for chloroform and carbon tetrachloride solutions and require no further comment. The carbonyl region, however, shows several features of interest (cf. Fig. 3). Pyridine evidently competes with the carbonyl group in forming a hydrogen bond with the phenolic group and, in the case of salicylaldehyde (cf. ref. 5), gives rise to a new, unchelated aldehydic carbonyl band at 1682 cm.$^{-1}$: the markedly lower frequency than is found for benzaldehyde in pyridine (1707 cm.$^{-1}$) is attributed to electron-donation from pyridine to the phenol group. As similar disruption of the intramolecular bond occurs in 5-t-butylsalicylaldehyde, and is almost complete in the 5-nitro-derivative (No. 8): this is regarded as ensuing from the mesomeric effect of the nitro-group on the phenol acidity, since in relatively non-basic solvents (CCl_4, $CHCl_3$: Table 1) the chelation

TABLE 4. *Carbonyl and nitro-absorptions (pyridine solutions).*[p]

No.	Substituents	ν_{CO}	$\Delta\nu_{\frac{1}{2}}$ [a]	ε_a	ν_{NO_2}	$\Delta\nu_{\frac{1}{2}}$ [a]	ε_a	ν_{NO_2}	$\Delta\nu_{\frac{1}{2}}$ [a]	ε_a
Salicylaldehydes										
1	None	1682	13 †	345	—	—	—	—	—	—
		1664	*	400						
		1646 [q]	*	195						
2	5-Bu^t	1677	13 †	325	—	—	—	—	—	—
		1654	20 †	395						
5	3-Bu^t, 6-Me	1634	30 ‡	480	—	—	—	—	—	—
8	5-NO_2	1688	14	560	1527	*	135	1343	11	1035
		(1666)	*	<165						
11	3-Bu^t, 5-NO_2, 6-Me	1640	24	320	1521	20	340	1337	*	380
12	3-NO_2	1692	14	375	1532	24	325	1351	*	240
		(1670)	*	(200)						
2-Hydroxyacetophenones										
19	None	1642	17	515	—	—	—	—	—	—
23	5-NO_2	1650	23	345	1528	17	255	1344	12	825
		1677	*	150						
24	3-NO_2	1654	21	350	1530	17	525	1361	23	345
		1683	*	<110						
Methyl salicylates										
40	None	1678	17	465	—	—	—	—	—	—
25	5-NO_2	1684	20	470	1528	19	365	1343	11	995
		1735	*	120				1356	14 †	390
26	3-NO_2	1685	16	415	1532	16	610	1347	*	280
								1335	*	280

[p] Approx. 0·05M in 0·11 mm. cells. [q] Not regarded as a carbonyl band. For symbols see Table 1.

in 5-nitrosalicylaldehyde appears to be as complete as that in salicylaldehyde. Inhibition of pyridine–phenolhydrogen bonding by steric effects is illustrated by 6-methyl-3-t-butylsalicylaldehyde (No. 5) and its 5-nitro-derivative (No. 11), which exhibit single chelated carbonyl bands, similar in frequency and intensity to those observed in chloroform solution.

Comparison of salicylaldehyde, 2-hydroxyacetophenone, and methyl salicylate shows that only the *ortho*-hydroxy-aldehyde chelation is disturbed by pyridine. This is in accord with the stability order of the intramolecular hydrogen bonds in these three types of compound as implied by the relative extent of competitive bonding by 3-nitro-groups described above [and by the frequency displacements corresponding to the introduction of *o*-OH into the parent compounds Ph·CO·R: R = H, −40; R = Me, −47; R = OMe, −46 cm.$^{-1}$ (CCl_4)]. However, introduction of a 5-nitro-substituent enhances the phenol

acidity sufficiently to permit a partial breaking of the intramolecular bonds in both the ketone (No. 23) and the ester (No. 25).

The results described above emphasise the need for care in interpreting the solution spectra of polyfunctional compounds in which different arrangements of hydrogen bonds are possible. In some cases the occurrence of a predominant chelated system may be recognised and the conformations of contiguous groups thereby determined. In general, the spectra must be considered in terms of all the possible conformations of the molecule, with due attention to the influences of intramolecular steric and electronic interactions and of the solvent. These effects may be profound in polarisable systems, as illustrated by the aromatic derivatives discussed in this paper.

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659. *Chemistry of Micrococcin* P. *Part V.*[1] *The Infrared Absorption Spectra of Thiazoles.*

By (MRS.) M. P. V. MIJOVIĆ and JAMES WALKER.

The infrared absorption spectra in the 2000—650 cm.$^{-1}$ region of 73 thiazoles of known structure and of 5 of partly known structure are discussed.

COMPARATIVELY few studies have been reported on the infrared spectra of thiazoles. Randall, Fowler, Fuson, and Dangl[2] examined the spectra of four thiazoles (48, 57, 75, 76 * in Table 1) in the range 3510—1100 cm.$^{-1}$ and observed absorption bands in the 1634—1570 cm.$^{-1}$ region (" thiazole I " band) and in the 1538—1493 cm.$^{-1}$ region ("thiazole II " band), which they regarded as being typical of the thiazole structure, although two of their compounds (48, 57) contained an amino-group, the deformation mode of which would be expected in the 1650—1590 cm.$^{-1}$ region. A systematic investigation of the infrared spectra of thiazole (1) and of five methyl derivatives (2—6) has been reported by Taurins, Fenyes, and Jones,[3] who, for purposes of analysis, divided the spectrum into eight regions. Of these, the 1690—1480 cm.$^{-1}$ region was assigned to skeletal vibrations of the thiazole ring, and this region includes the " thiazole I " and " thiazole II " bands of Randall *et al.*[2] In the 1445—1375 cm.$^{-1}$ region they concluded that bands at 1445 and 1435 cm.$^{-1}$ arose only from absorption of the methyl groups and that bands in the range 1385—1375 cm.$^{-1}$ were given by the thiazole skeleton in addition to the methyl groups. Bands in the 1340—1175 cm.$^{-1}$ region, with the exception of bands at 1192—1175 cm.$^{-1}$, were assigned to skeletal vibrations of the thiazole ring, as were those in the 1160—930 cm.$^{-1}$ region. The bands in the remaining region, namely 900—640 cm.$^{-1}$, were associated with out-of-plane bending vibrations of the C–H groups of the thiazole ring, but no correlation was noted between the number of bands observed and the number of hydrogen atoms attached directly to the thiazole ring.

About the same time, Sheinker, Kushkin, and Postovskii[4] reported the infrared spectra of a number of 2-aminothiazoles and their derivatives (48—53, 56), and also discussed the

* These and similar Arabic numerals in parentheses refer to the numbers of compounds in the Tables.

[1] Part IV, Brookes, Clark, Majhofer, Mijović, and Walker, *J.*, 1960, 925.
[2] Randall, Fowler, Fuson, and Dangl, " Infra-red Determination of Organic Structures," D. Van Nostrand Co., Inc., New York, 1949.
[3] Taurins, Fenyes, and Jones, *Canad. J. Chem.*, 1957, **35**, 423.
[4] Sheinker, Kushkin, and Postovskii, *Zhur. fiz. Khim.*, 1957, **31**, 214.

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spectra of thiazole (1), some simple methylthiazoles (2, 3, 5, 7) and 2-bromothiazole (9). The infrared spectra of several 2-aminothiazoles [5] (48, 51, 56) and 2-acetamidothiazoles [6] (68—73) had been reported earlier; some of these spectra were measured in mineral oil only (68—73), which masked part of the " thiazole II " region of Randall *et al.*[2] The resolution,[4-6] especially in the lower frequency range, was poor, and no bands below 770 cm.$^{-1}$ were recorded. In a study of the infrared spectra of fifteen 2-substituted thiazolines, Otting and Drawert [7] observed the spectra of 2-methyl-, 2-phenyl- (10), and 2-benzylthiazole, and noted that the intensity of the bands in the " thiazole I " region was very weak in these compounds, in contrast with the thiazolines which showed intense C=N absorption in the 1640—1550 cm.$^{-1}$ region. Katritzky [8] has pointed out that heteroaromatic compounds containing five-membered rings generally show three bands in the 1600—1350 cm.$^{-1}$ region, near 1590, 1490, and 1400 cm.$^{-1}$, due to ring-stretching modes, and quoted 1610, 1500, and 1380 cm.$^{-1}$ as approximate frequencies for substituted thiazoles on the basis of the Canadian work.[3]

The thiazole nucleus contains the conjugated –C=C–N=C– system. As a result of work on aliphatic polyene azines, it has been pointed out by Blout, Fields, and Karplus [9] that, with increasing conjugation, observed frequencies no longer correspond to the vibration of an individual bond, and, when the bonds are no longer alike, the assignment of the vibrations to the oscillation of individual structures, or even to certain combinations of such oscillations, becomes impossible. Bellamy,[10] when discussing C=N stretching vibrations, emphasises that the C=N absorptions of conjugated cyclic systems cannot be considered alone, as they interact with other double bonds to a much greater extent than they do in open-chain compounds. Furthermore, the frequencies of C=C and C=N links are so close that when they are present in a ring it is doubtful whether either can be regarded as retaining its original character. In conjugated cyclic systems extensive shifts of both C=C and C=N absorptions can occur and it is better to consider the group of absorptions as a whole in relation to the particular structural unit concerned. Similar conclusions concerning the ring vibrations of pyrimidines have been drawn by Short and Thompson [11] and by Angyal and Werner.[12] Katritzky [8] has classified the molecular vibrations of heteroaromatic compounds containing planar five- and six-membered rings, basing his discussion of the skeletal modes for five-membered rings on thiophen, furan, and pyrrole; these were divided into skeletal stretching modes at *ca.* 1600—1250 cm.$^{-1}$, the ring-breathing frequency at *ca.* 1150—800 cm.$^{-1}$, in-plane bending at *ca.* 900—600 cm.$^{-1}$ and out-of-plane bending at *ca.* 600—450 cm.$^{-1}$.

During work on micrococcin *P*, described in Part IV [1] and earlier papers [13] of this series, we have had occasion to observe the infrared spectra of a considerable number of mono- and di-substituted thiazoles and polythiazolyls in potassium chloride discs, and sometimes additionally in chloroform, over the range 2000—650 cm.$^{-1}$. Altogether the infrared spectra of 53 mono- and poly-substituted thiazoles have been observed (including those of micrococcin *P* and of four of its derivatives whose structures are only partially known) and the results, together with data for a further 25 thiazoles abstracted from the literature are summarised in Tables 1—3. For the sake of convenience the spectrum has been divided into five sections, namely, 1800—1475, 1475—1350, 1350—1175, 1175—930, and 930—650 cm.$^{-1}$, and these will be discussed individually. The Tables have been still further subdivided for ease of reference.

[5] Bogomolov, Sheinker, and Postovskii, *Zhur. obshchei Khim.*, 1954, **24**, 539.
[6] Bogomolov, Sheinker, and Postovskii, *Doklady Akad. Nauk S.S.S.R.*, 1953, **93**, 277.
[7] Otting and Drawert, *Chem. Ber.*, 1955, **88**, 1469.
[8] Katritzky, *Quart. Rev.*, 1959, **13**, 353.
[9] Blout, Fields, and Karplus, *J. Amer. Chem. Soc.*, 1948, **70**, 194.
[10] Bellamy, " The Infra-red Spectra of Complex Molecules," 2nd edn., Methuen & Co., Ltd., London, 1958, p. 270.
[11] Short and Thompson, *J.*, 1952, 168.
[12] Angyal and Werner, *J.*, 1952, 2911.
[13] (a) Brookes, Fuller, and Walker, *J.*, 1957, 689; (b) Mijović and Walker, *J.*, 1960, 906; (c) Brookes, Clark, Fuller, Mijović, and Walker, *J.*, 1960, 916.

TABLE 1. *Absorption bands in the* 1800—1475 cm.$^{-1}$ *region.*

Compound Ref. Phase 1800—1700 1700—1634 1634—1535 1535—1475

TABLE 1. *Absorption bands in the* 1800—1475 cm.$^{-1}$ *region.*

No.	Compound	Ref.	Phase	1800—1700	1700—1634	1634—1535	1535—1475
1	Thiazole	3	Film			*1615*m	*1485*vs
		4	Film				*1485*s
2	2-Methylthiazole	3	Film			*1605*w	*1505*vs
		4	Film				*1505*s
3	4-Methylthiazole	3	Film			*1610*sh	*1520*vs, *1485*w
		4	Film				*1518*s
4	5-Methylthiazole	3	Film				*1530*s
5	2,4-Dimethylthiazole	3	Film		*1690*w	*1620*w	*1530*vs, *1480*vs
		4	Film				*1532*s
6	2,5-Dimethylthiazole	3	Film		*1675*w	*1537*s	*1482*s
7	2,4,5-Trimethylthiazole	4	Film			*1556*m	*1486*s
8	5-(2-Hydroxyethyl)-4-methylthiazole		Film		1640vw	1543m	
9	2-Bromothiazole	4	Film				*1482*s
10	2-Phenylthiazole	7	KBr			*1600*w	*1515*m, *1493*vs
11	2,5-Diphenylthiazole	[a]	CCl_4 }			*1600*m, *1575*w,	*1527*m, *1481*vs
			CS_2 }			*1550*w	
12	Methyl thiazole-4-carboxylate	13c	KCl	1715vs		1571w	1501s, 1490sh
			$CHCl_3$	1725s		1605w	
13	Methyl 2,4′-bithiazolyl-4-carboxylate	13c	KCl	1735vs		1543m	1485m
			$CHCl_3$	1725s		1605w	
14	Methyl 2,4′:2′,4″-terthiazole-4-carboxylate	13c	KCl	1715vs		1535w	1495m
			$CHCl_3$	1725s		1605w	
15	Methyl 2,4′:2′,4″:2″,4‴-quaterthiazole-4-carboxylate	13c	KCl	1730sh, 1705vs	1670m	1545w	1500m, 1480m
16	Dimethyl 2,2′-methylenebisthiazole-4,4′-dicarboxylate		KCl	1715vs		1600w	1502s
17	Dimethyl 2,2′-*p*-phenylenebisthiazole-4,4′-dicarboxylate		KCl	1720vs	1675sh	1625m, 1575w	1528w, 1496m, 1482m
18	C_{24} dimethyl ester	13a, c	KCl	1735s, 1718vs	1680s	1580m, 1555w	1510w, 1485m
			Nujol	1730m, 1715s	1680m	1585m, 1555vw	1505sh
			$CHCl_3$	1720s	1685m	1590m	
19	C_{22} dicarboxylic acid corresponding with 18	13b	KCl	1700vs	1685vs	1588m, 1560w, 1535vw	1488m
20	C_{23} diol derived from C_{24} dimethyl ester	13c	KCl			1577m, 1560m	1505sh, 1490m
21	4-Hydroxymethyl-2,4′-bithiazolyl	1	KCl				1525m
22	4-Bromomethyl-2,4′-bithiazolyl		KCl				1530m, 1500m, 1485m
23	Methyl 2-carbamoylthiazole-4-carboxylate	13c	KCl	1732s	1685s, 1665s	1605m	1490m
			$CHCl_3$	1725s	1695sh	1605m, 1580w	1475m
24	Thiazole-4-carbonamide	13c	KCl		1640vs	1605s	1515m
			$CHCl_3$		1685vs	1605sh, 1575s	
25	2,4′-Bithiazolyl-4-carbonamide	13c	KCl		1675vs	1595m	1510w
			$CHCl_3$		1683s	1605sh, 1580vs	1480m
26	2,4′-Bithiazolyl-4-carbohydrazide		KCl		1650s	1615s, 1535s	1480m
27	2-Aminothiazole-4-carbohydrazide		KCl		1645sh	1620s, 1540s	1490m
28	2-Hydrazinothiazole-4-carbohydrazide		KCl		1660s	1625s, 1580s	1518s
29	Thiazole-2,4-dicarboxylic acid	13a	KCl	1715vs	1680vs		1495m
30	Thiazole-4-carboxylic acid	13a	KCl		1675s		1490m
31	2,4′-Bithiazolyl-4-carboxylic acid		KCl		1695vs		1515m
32	2-Phenylthiazole-4-carboxylic acid	1	KCl		1670vs		1485m
33	4-Cyanothiazole	13c	KCl			1625vw	1475w

TABLE 1. (*Continued.*)

No.	Compound	Ref.	Phase	1800—1700	1700—1634	1634—1535	1535—1475
34	4-Cyano-2,4′-bithiazolyl	13c	KCl			1625vw	1530m, 1475w
35	Thiazole-4-carbothioamide	13c	KCl			1615vs	1505m
36	2,4′-Bithiazolyl-4-carbothioamide	13c	KCl			1595s	1525vw
37	Methyl 2-acetylthiazole-4-carboxylate	13c	KCl	1725vs	1695s		1500w, 1475m
38	Methyl 2-propionylthiazole-4-carboxylate	13a	KCl	1730vs	1690s		1500w, 1480sh
39	Methyl 2-bromoacetylthiazole-4-carboxylate	13c	KCl	1720vs	1695s		1480m
40	2-Propionylthiazole-4-carboxylic acid	13a	KCl		1680vs		
41	2-Isobutyrylthiazole-4-carboxylic acid	13a	KCl		1680vs		1480m
42	Methyl 2-1′-hydroxy-n-propylthiazole-4-carboxylate		KCl	1720vs			1510sh, 1500s
43	2-1′-Hydroxyethylthiazole-4-carboxylic acid	13c	KCl		1685vs		1495m
44	2-(1-Hydroxy-2-methylpropyl)thiazole-4-carboxylic acid	13a	KCl		1700vs		1495m
45	2-Aminomethylthiazole-4-carboxylic acid hydrochloride	1	KCl		1700s	1570m	1490s
46	2-1′-Aminoethylthiazole-4-carboxylic acid hydrochloride	1	KCl		1695s	1605m, 1580m	1490s
47	2-(1-Amino-2-methylpropyl)thiazole-4-carboxylic acid hydrochloride	1	KCl		1700vs	1595m, 1580sh	1505vs, 1480m
48	2-Aminothiazole		KCl			1625vs	1520s, 1490s
		5	Min. oil			*1626*s	*1515*s
		2	Nujol			*1626*s	*1515*s, *1484*s
		12	$CHCl_3$			*1605*m	*1523*s, *1486*m
		4	Min. oil *			*1627*s	*1523*s
49	2-Methylaminothiazole	4	Film			*1600*sh, *1546*vs	
50	2-Dimethylaminothiazole	4	Film			*1560*s	
51	2-Amino-4-methylthiazole	5	Film			*1622*m	*1516*s
		4	Min. oil *			*1616*m	*1522*s
52	2-Dimethylamino-4-methylthiazole	4	Film			*1565*s	
53	2-Amino-4,5-dimethylthiazole	4	Min. oil *			*1613*m	*1532*s
54	2,2′-Diamino-4,4′-tetramethylenebisthiazole	[b]	KCl			1609vs	1530sh, 1513vs
55	2,2′-Diamino-4,4′-hexamethylenebisthiazole	[b]	KCl			1609vs	1530sh, 1510vs
56	2-Amino-4-phenylthiazole	5	Min. oil			*1598*m	*1523*m
		4	Min. oil *			*1592*s, *1537*s	*1500*m
57	2-Amino-4-*p*-biphenylylthiazole	2	Nujol			*1634*m, *1605*w	*1538*m, *1522*m
58	Ethyl 2-aminothiazole-4-carboxylate	[c]	KCl		1695s	1620s	1535s
			$CHCl_3$	1715vs		1607s	1520m
59	Ethyl 2-benzamidomethylthiazole-4-carboxylate	1	KCl	1708s	1640s	1605w, 1580m	1530s, 1500s, 1490sh
			$CHCl_3$	1720vs	1660s	1605s, 1585m	1485s
60	Ethyl 2-(1-benzamido-2-methylpropyl)thiazole-4-carboxylate	1	KCl	1705s	1635s	1600w, 1575m	1520s, 1485s
			$CHCl_3$	1723vs	1658s	1605m, 1583m	1483s
61	2-1′-Benzamidoethyl-4-benzylthiazole		KCl		1635s	1600m, 1575m	1520s, 1490m
62	2-(1-Benzamido-2-methylpropyl)-4-phenylthiazole	[d]	KCl		1640vs	1608m, 1585m	1520vs, 1485s
63	2-1′-Aminoethyl-4-phenylthiazole hydrochloride	1	KCl			1575m	1490vs
64	2-(1-Amino-2-methylpropyl)-4-phenylthiazole hydrochloride	[d]	KCl			1605s	1498s
65	2,4-Diamino-5-phenylthiazole hydrochloride	[e]	KCl		1675m	1634s	1490s
66	2,4-Diamino-5-phenylthiazole	[e]	KCl		1655w	1630sh, 1605s	1515s, 1490sh
67	2,4-Diamino-5-*p*-chlorophenylthiazole	[e]	KCl			1630sh, 1605m	1515s, 1490m
68	2-Acetamidothiazole	6	Min. oil		*1668*m	*1551*s	
69	2-Acetamido-4-methylthiazole	6	Min. oil		*1682*s	*1550*m	
70	2-Acetamido-4,5-dimethylthiazole	6	Min. oil		*1685*m	*1542*s	

TABLE 1. (*Continued.*)

No.	Compound	Ref.	Phase	1800—1700	1700—1634	1634—1535	1535—1475

69	2-Acetamido-4-methylthiazole	6	Min. oil		*1682*s	*1550*m
70	2-Acetamido-4,5-dimethylthiazole	6	Min. oil		*1685*m	*1542*s

TABLE 1. (*Continued.*)

No.	Compound	Ref.	Phase	1800—1700	1700—1634	1634—1535	1535—1475
71	2-Acetamido-4-phenylthiazole	6	Min. oil		*1648*m	*1561*s	
72	2-Acetamido-5-bromo-4-methylthiazole	6	Min. oil		*1658*m	*1561*s	
73	2-Acetmethylamido-4-methylthiazole	6	Min. oil		*1648*m	*1542*w	*1500*s
74	2-Sulphanilamidothiazole (Sulphathiazole)		KCl			1595m, 1573m	1528s, 1495m
75	4,5-Dimethylthiazole-2-thiol	2	Nujol			*1623*m, *1605*m	*1479*s
76	4-Phenylthiazole-2-thiol	2	Nujol			*1590*m, *1570*m	*1511*w, *1493*s
77	Micrococcin *P*	13a, c	KCl		1655s	1580sh	1530s, 1480m
78	Tetra-acetylmicrococcin *P*	13b	KCl	1735m	1665s	1575w	1525s

All italicised data were obtained from the literature.

vs = very strong; s = strong; sh = shoulder; m = medium; w = weak; vw = very weak; Min. oil = mineral oil; "Min. oil *" indicates that a polyfluorohydrocarbon was used for the range 2000—1350 cm.$^{-1}$ and mineral oil for the range 1350—770 cm.$^{-1}$.

References: [a] Koenig, Hayes, Rogers, and Perrings, U.S. Atomic Energy Commn., AECU-2778, 1953. [b] Walker, *J.*, 1940, 1304. [c] Steude, *Annalen*, 1891, **261**, 26. [d] Dean, Mijović, and Walker, following paper. [e] Chase and Walker, *J.*, 1955, 4443.

TABLE 2. *Absorption bands in the* 1475—1175 cm.$^{-1}$ *region.*

No.	Ref.	Phase	1475—1350	1350—1250	1250—1175
1	3	Film	*1385*vs	*1320*vs	*1240*vs
2	3	Film	*1435*vs, *1413*s, *1376*s	*1310*s, *1285*vw	*1210*m, *1187*vs
3	3	Film	*1445*vs, *1414*vs, *1375*s	*1340*vw, *1307*vs	*1235*w, *1220*w, *1185*w
4	3	Film	*1445*m, *1405*s	*1305*vw	*1240*s, *1175*s
5	3	Film	*1445*vs, *1380*vs	*1305*vw	*1220*vw, *1185*vs
6	3	Film	*1445*vs, *1402*w, *1376*s	*1290*s	*1210*sh, *1188*vs
7	4	Film	*1443*s, *1374*m	*1306*m	*1195*s
8		Film	1470sh, 1445sh, 1415s, 1380m	1312m	1240m, 1195w
9	4	Film	*1390*vs	*1300*m	*1195*w
10	7	KBr	*1454*m, *1418*m	*1333*w, *1324*m, *1290*w, *1265*vw	*1250*s, *1178*vw
11	[e]	CCl_4 / CS_2	*1451*s, *1425*m	*1332*m, *1312*w, *1268*m, *1258*m	*1234*w, *1180*w
12	13c	KCl	1430m, 1410m	1325m, 1275s	1215s
13	13c	KCl	1468s, 1430m, 1408m	1345m, 1315s	1240s, 1215vs, 1180s
14	13c	KCl	1470s, 1438m, 1422w, 1395s	1330w, 1315s, 1290m	1245vs, 1215sh, 1205sh, 1190sh
15	13c	KCl	1460m, 1435m, 1380s	1330w, 1310m, 1275w	1245s
16		KCl	1470s, 1435m, 1420m	1318s, 1300m	1245s, 1195sh
17		KCl	1462vs, 1430m, 1404m	1345s, 1330m, 1290m	1240vs
18	13a, c	KCl	1445s, 1410w, 1375m	1340m, 1320w, 1300w	1245s, 1208vs, 1180sh
19	13b	KCl	1455m, 1408m, 1375m	1330m, 1300w	1243s, 1223s, 1185m
20	13c	KCl	1463w, 1435s, 1415s, 1375vw, 1355w	1350m, 1310m, 1255m	1200m
21	1	KCl	1448w, 1400s, 1368m	1320w, 1300m	1220m, 1185m
22		KCl	1415w, 1395m	1325m, 1300m	1230m, 1205s, 1175m
23	13c	KCl	1475m, 1433m, 1385m	1340s	1233s
24	13c	KCl	1450w, 1430s, 1363s	1315s	1220w
25	13c	KCl	1460m, 1396m, 1363m	1315m, 1285m	1243w, 1175m
26		KCl	1465sh, 1410m	1305m, 1270m	1248w, 1230w, 1190m
27		KCl		1342m, 1320w, 1290vw, 1265m	
28		KCl	1413m, 1355m	1350m, 1280s	
29	13a	KCl	1460w, 1440m, 1380w	1320m, 1278s	1205s
30	13a	KCl	1440m, 1390w	1335m, 1278s	1210s

TABLE 2. (*Continued.*)

No.	Ref.	Phase	1475—1350	1350—1250	1250—1175
31		KCl	1460m, 1405m	1314w	1215s, 1178m
32	1	KCl	1465m, 1440m, 1405m	1335m, 1310sh, 1252m	1218s
33	13c	KCl	1420s	1298s	1210m
34	13c	KCl	1460sh, 1405s	1317s, 1260vw	1240m, 1180m
35	13c	KCl	1455w, 1435s, 1415s	1340m, 1275m	1245m, 1190m
36	13c	KCl	1460w, 1390s	1310m	1240vw, 1175m
37	13c	KCl	1458m, 1430m, 1410m, 1362m	1333s, 1295m, 1275s	1225vs, 1180m
38	13a	KCl	1458m, 1433m, 1410m, 1380w, 1360m	1336s, 1280w	1220vs
39	13c	KCl	1458s, 1430m, 1392m	1315s, 1295m, 1270m	1230vs, 1185s
40	13a	KCl	1472m, 1405m, 1385m, 1358m	1336m, 1280m	1250s, 1225s
41	13a	KCl	1458m, 1400m, 1390m, 1370w	1335s, 1280m	1245s, 1220s
42		KCl	1460m, 1440m, 1375w	1330s, 1300m, 1285vs	1235vs, 1175s
43	13 [e]	KCl	1414m, 1368m	1340w, 1320w, 1275m	1243s
44	13 [e]	KCl	1475sh, 1390m, 1370sh	1325w, 1280w	1215s
45	1	KCl	1440m, 1395m	1305m	1210vs
46	1	KCl	1473m, 1385m, 1355m	1305m	1218vs
47	1	KCl	1385m	1300w, 1273w	1220vs, 1195sh
48		KCl	1400w, 1358m	1320m, 1275m	1200s
49	4	Film	*1400*s	*1327*m	*1235*m, *1189*m
50	4	Film	*1425*m	*1345*m, *1252*m	
51	5	Film	*1440*w, *1380*m	*1317*m	
52	4	Film	*1427*m, *1379*w	*1342*s, *1288*m	*1234*m
53	4	Min. oil [e]	*1390*m	*1316*m	
54	[b]	KCl	1455m, 1425m, 1376m	1315sh, 1305s, 1275m	1205m
55	[b]	KCl	1460m, 1442w, 1428m, 1380m	1330m, 1300s, 1280m	1200w
56	5	Min. oil.		*1335*m, *1283*m	*1200*w
57	2	Nujol	*1404*m, *1355*m	*1333*m, *1309*w, *1292*vw	*1202*w
58	[e]	KCl	1470m, 1442m, 1370s	1336s	1248s
59	1	KCl	1468m, 1450m, 1438m, 1393m, 1366m	1345m, 1315s, 1272m	1240s, 1185w, 1175w
60	1	KCl	1442m, 1392m, 1366m	1327m, 1315m, 1285m	1242s, 1185m
61		KCl	1456m, 1430m, 1385w	1337m, 1315m, 1305s, 1272m	1215m
62	[d]	KCl	1470m, 1445m, 1385m	1330m, 1318m, 1285s	1240w, 1180m
63	1	KCl	1440m, 1380m, 1360m	1320m, 1290vw, 1273w	1210w
64	[d]	KCl	1460m, 1445m, 1395m	1345m, 1293w, 1275m	1232m, 1205w
65	[e]	KCl	1450w, 1418m, 1365w	1340m	1220w, 1178m
66	[e]	KCl	1455w, 1445m, 1375s	1325m, 1275w	1223m, 1188w
67	[e]	KCl	1405m, 1368s	1330m, 1300w, 1260w	1215w, 1185w
68	6	Min. oil		*1290*m	*1215*w, *1163*m
69	6	Min. oil		*1290*m	*1250*m, *1218*w
70	6	Min. oil		*1265*m	*1218*w
71	6	Min. oil		*1290*s	
72	6	Min. oil		*1334*m, *1282*m	
73	6	Min. oil		*1315*m, *1265*w	
74		KCl	1425s	1318m, 1280s, 1265s	
75	2	Nujol	*1445*s	*1321*m, *1263*m	*1206*w, *1185*m
76	2	Nujol	*1445*s	*1342*m, *1316*w, *1305*vw, *1282*m, *1253*w	*1203*w, *1186*m
77	13a, c	KCl	1445sh, 1420sh, 1380w	1310vw, 1275vw	1230m, 1185w
78	13b	KCl	1468m, 1445sh, 1420sh, 1370m	1310vw	1225s

[e]—[e] See Table 1.

TABLE 3. *Absorption bands in the* 1175—650 cm.$^{-1}$ *region.*

78	13b	KCl	1468m, 1445sh, 1420sh, 1370m	1310vw		1225s

— See Table 1.

TABLE 3. *Absorption bands in the* 1175—650 cm.$^{-1}$ *region.*

No.	Ref.	Phase	1175—1050	1050—930	930—800	800—700	700—650
1	3	Film	*1120*vs	*1040*vs	*880*vs, *860*vs	*800*vs, *720*vs	
2	3	Film	*1160*vs, *1055*m	*966*m, *930*s	*874*s, *830*m, *810*m	*763*s, *717*vs	
3	3	Film	*1135*m	*1037*m, *995*s, *930*vs	*875*vs, *830*vs, *807*vs	*727*s	*670*m
4	3	Film	*1107*s	*1035*w, *990*vw	*870*vs, *847*sh	*785*s	
5	3	Film	*1140*vs	*1015*s, *940*vs	*853*vs	*720*vs	*665*s
6	3	Film	*1160*vs	*990*m, *960*s	*840*vs	*757*s	*673*vw, *652*s
7	4	Film	*1066*m	*1020*m, *965*m	*875*m		
8		Film	1155w, 1055s	945w	920m, 857m	785m	
9	4	Film	*1145*m	*1047*m, *1006*vs	*870*m		
10	7	KBr	*1142*s, *1092*w, *1070*m, *1053*s	*1020*w, *1000*m, *970*vs	*917*w, *877*m, *836*vw	*757*vs, *719*m	*689*vs
11	*	CCl_4 / CS_2	*1152*s, *1100*w, *1075*m	*1033*m, *1005*m, *980*s, *962*m	*914*m, *903*w, *854*s	*757*vs	*684*s
12	13c	KCl	1090s	980s	910s, 880s, 860s, 830s	775m, 765s	
13	13c	KCl	1092s	983s	920w, 875s, 855s	785m, 765m, 735s	
14	13c	KCl	1090m	1015m, 985m	925m, 890m, 880w, 870s, 850m, 820m, 810w	790w, 765s, 745w	
15	13c	KCl	1095m	1035vw, 1015w, 995m, 930m	905m, 880s, 865sh, 830m	765s	
16		KCl	1158vs, 1080m, 1055m	988s, 938s	915m, 898m, 865s, 830s	783s, 765vs	
17		KCl	1118w, 1103vs	1020m, 1000s, 970s	905s, 875w, 860w, 850s, 840m	764s	
18	13a, c	KCl	1110m, 1095s, 1075w	1040vw, 1025w, 1015m, 1000w, 970w, 940m	915w, 890m, 852m, 844sh	800m, 795sh, 775sh, 760s, 742m	
19	13b	KCl	1110m, 1085w, 1060vw	1040vw, 1020w, 995w, 980m, 950m, 930m	890m, 855m, 845m	790m, 770w, 750m, 730s, 720sh	690vw, 670w
20	13c	KCl	1135w, 1112m, 1090w, 1065m	1050s, 1038s, 1020s, 990s, 960m, 930w	880vw, 865w, 850m	800w, 760s, 735m	
21	1	KCl	1150s	1050s, 1025vs, 955s	880vs, 820vs	785m, 750m	
22		KCl	1153s, 1100w	1025m, 963m	885m, 870s, 845s, 800m	742m, 720m	
23	13c	KCl	1123m, 1095m, 1080m	982m	915w, 870w, 815w	785s, 765s, 725w, 705s	660m
24	13c	KCl	1110m, 1085m	935s	885s, 840s, 825s	790s, 775m	680m
25	13c	KCl	1085w	1020w, 940m	875s, 843m	780m, 750w	700m
26		KCl	1100m	1035w, 995m, 940s	895w, 875vs, 850sh, 835s, 810m	780s, 720m	685m
27		KCl	1077m	995w, 945m	856w	800m	680m
28		KCl	1160w, 1110s	1035m, 990s, 945m	860w, 810m	790w	700m
29	13a	KCl	1135w, 1100m	940m	885w, 875w, 860w, 825w	765m, 735m	
30	13a	KCl	1110m	940s	880m, 855m, 820m	775m, 735m	
31		KCl	1110sh	1030vw, 940m	880m, 860vw, 825m	765w, 725m	
32	1	KCl	1095m	1025vw, 990m	912w, 870w, 805w	770sh, 757m, 740m	680m
33	13c	KCl	1128m	935s	885s, 835s	775m	
34	13c	KCl	1150m	1025vw, 950s	886s, 878s, 840s, 805w	784m, 765sh, 755w, 705w	
35	13c	KCl	1110m	955vs	885s, 865s, 835s, 810s	780m, 750m	700s
36	13c	KCl	1075m	1025m, 960s	875s, 825s	775s	
37	13c	KCl	1115w, 1098m, 1060m	1015m, 980m, 935m	915m, 870vw, 855w, 825m	780s, 770s	
38	13a	KCl	1105m, 1085m	1010w, 995s, 930m	900s, 840m, 800vw	775s, 735w	
39	13c	KCl	1100m, 1055w	990m, 950m	915m, 875w, 835w	773s	

TABLE 3. (*Continued.*)

No.	Ref.	Phase	1175—1050	1050—930	930—800	800—700	700—650
40	13a	KCl	1105m, 1085m	1005w, 950s	900s, 828m	798m, 765s, 750s	
41	13a	KCl	1105m	960s	924s, 885m, 835m	770m, 752s, 710w	
42		KCl	1120m, 1100m, 1080m, 1065w	1050m, 980s	920m, 883w, 870m, 862m, 820w, 810w	785m, 762s, 720m	
43	13c	KCl	1100m, 1060m	1015m	925m, 885w, 860w, 810w	755s, 745s	
44	13a	KCl	1100m	1045m, 1015m, 950m	865w, 805w	745s	
45	1	KCl	1095m, 1058m	980m	843s, 815m	760m, 715m	692m
46	1	KCl	1095m	1045m, 940w	875w, 845s, 815m	760m, 728s	680m
47	1	KCl	1098w, 1060m	980m, 945m	910vw, 870m, 820s	758vw, 715s	700m
48		KCl	1155sh, 1065w	1030s	880m, 860w	755m, 703s	685s
49	4	Film	*1130*m, *1061*m	*950*w	*861*m	*755*m	
50	4	Film	*1160*w, *1118*s, *1110*m, *1055*s	*932*m	*885*w, *865*m		
51	5	Film	*1105*w	*968*m			
52	4	Film	*1126*s, *1068*m	*1020*s, *986*m	*930*w, *914*m, *839*m		
53	4	Min. oil [a]	*1142*m, *1119*m	*980*m	*872*m		
54	[b]	KCl	1105m	1025m, 965m	910w, 850m	735s	690vs
55	[b]	KCl	1105m	1050m, 1005m, 970m	845w	780w, 725s	690vs
56	5	Min. oil	*1064*w	*1036*m	*910*m, *850*m		
57	2	Nujol	*1111*w				
58	[c]	KCl	1115m, 1075m	1020s, 972s	875s, 852w, 820w	783s, 745s	680m
59	1	KCl	1140m, 1095s, 1075w	1050w, 1030w, 1015s, 980m, 940m	925w, 875s, 855w, 840m, 825w, 813w, 805w	772m, 756s, 725s	694vs
60	1	KCl	1143m, 1095m, 1075w, 1055w	1025m, 953m	925w, 882s, 860vw, 830m	800m, 790m, 765s, 726s	690vs
61		KCl	1150m, 1120m, 1080m, 1070m	1025m, 995m, 960m	930w, 900w, 865m, 810m	765sh, 755s, 735s, 715vs	695s
62	[d]	KCl	1170m, 1140m, 1070m, 1060m	1050w, 1025m, 1000w, 940m	925m, 910m, 888w, 855m, 823m, 800m	770m, 730sh, 715s, 700m	685s
63	1	KCl	1035s, 1070m	1050s, 1025w, 965w	910m, 845m	790m, 756s, 740sh	682s, 675s
64	[d]	KCl	1155w, 1115w, 1085m, 1070m, 1055m	1045s, 1025m, 998m	915m, 853m	775w, 738vs	695sh, 682m
65	[e]	KCl	1075w, 1055m		895vw, 855vw	790sh, 750s	690s
66	[e]	KCl	1160w	1015m, 995w, 950w	880m, 810vw	750s	690s
67	[e]	KCl	1125w, 1095m	1010m, 950w	880w, 815s		
68	6	Min. oil	*1156*m, *1065*m	*1037*w, *961*m			
69	6	Min. oil		*1020*w, *1005*m, *934*m	*847*m		
70	6	Min. oil		*1015*m	*893*m		
71	6	Min. oil		*1032*m, *990*m	*897*m, *847*m		
72	6	Min. oil		*1047*m, *1010*m, *985*m			
73	6	Min. oil	*1150*s, *1075*w	*1005*s	*840*m		
74		KCl	1135vs, 1088m	1015w	920s, 850m, 830w, 810m	725m	700w, 665s
75	2	Nujol	*1140*w, *1105*m				
76	2	Nujol	*1151*w, *1146*w				
77	13a, c	KCl	1115m, 1075m	1045m, 1020m, 995m, 970w, 940m	880w, 840m	745s	
78	13b	KCl	1060m	1045m, 1013m, 988w, 950w	925vw	738m	

[a]—[e] See Table 1.

The 1800—1475 cm.$^{-1}$ *Region* (Table 1).—(a) 1800—1700 cm.$^{-1}$ *region.* The only bands observed in this region are due to ester C=O stretching vibrations, or, in two cases (19, 29), to carboxyl-carbonyl stretching modes. All the esters examined are either ethyl or methyl esters, and all contain the ester group as a substituent in the 4-position of the thiazole nucleus (12—17, 23, 37—39, 42, 58—60). In the solid state the majority absorb between 1735 and 1715 cm.$^{-1}$; Bellamy [14] cites 1730—1717 cm.$^{-1}$ as the usual range for aryl esters. The four compounds (15, 58—60) exhibit unusually low ester-carbonyl frequencies, absorbing in the region 1708—1695 cm.$^{-1}$. Three of these (58—60) were investigated in chloroform solution (0·25—0·7%) and the ester-carbonyl absorption then shifted to the range 1723—1715 cm.$^{-1}$, suggesting that some intermolecular bonding may be occurring in the solid state. Similarly, compounds (12—14) showed a fairly wide variation in ester-carbonyl absorption in the solid state for a series of such closely related compounds, but investigation of the spectra in chloroform solution (0·5%) showed a constant ester-carbonyl frequency of 1725 cm.$^{-1}$ for all these compounds. Eisner and Erskine [15] in their work on the infrared spectra of pyrrolecarboxylic esters also noted that solid-state spectra do not show uniform frequencies even among similar compounds, since the carbonyl stretching frequency depends upon the packing and hydrogen bonding of the molecules within the crystals.

(b) 1700—1535 cm.$^{-1}$ *region.* This region includes the " thiazole I " region (1634—1570 cm.$^{-1}$) originally postulated by Randall *et al.*[2]. Thiazole (1) itself shows a band of medium intensity at 1615 cm.$^{-1}$, but inspection of Table 1 reveals that bands in this region are shown only by certain types of thiazoles, although they may well be masked in certain other thiazole derivatives. For those compounds (1—3, 5—8, 12—16, 23—25, 33, 34, 49, 50, 52, 75) where the " thiazole I " band does appear, it is usually weak, and rarely of medium or strong intensity, and the lower end of the range appears to be around 1535 cm.$^{-1}$. For the nitriles (33, 34), amides (23—25) in chloroform, esters (12—14) in chloroform, thiazole (1) itself, simple methylthiazoles (2, 3, 5), and 4,5-dimethylthiazole-2-thiol (75), it is usually a weak band occurring between 1625 and 1605 cm.$^{-1}$, while for esters (12—16) in the solid state it is a band of weak or medium intensity between 1600 and 1535 cm.$^{-1}$. For a limited number of alkylthiazoles (6—8) and alkylaminothiazoles (49, 50, 52) the " thiazole I " band apparently appears as a medium or strong band in the region of 1565—1537 cm.$^{-1}$. This is in agreement with the observation by Otting and Drawert [7] that the intensity of the " thiazole I " bands in the three compounds which they investigated was very weak.

In all the other thiazole derivatives investigated, where bands are observed in this region, it is found that these are caused by the absorption of one or more of the substituent groups. In certain aryl derivatives (10, 11, 17, 76) absorption in the region of 1600—1575 cm.$^{-1}$ is probably due to the C=C stretching vibrations of the benzene rings.[16]

In the amide derivatives (23—25) the strong bands in the region 1685—1640 cm.$^{-1}$ are assigned as primary amide I bands. This is substantiated by a shift to a higher frequency in chloroform solution (0·3%).[17] In methyl 2-carbamoylthiazole-4-carboxylate (23) the nature of the strong band appearing at 1665 cm.$^{-1}$ in the solid state is not clear—this band disappears in chloroform solution and is sometimes absent from spectra taken from potassium chloride discs. In chloroform solution the bands at 1605, 1605, and 1595 cm.$^{-1}$ of compounds (23), (24), and (25), respectively, resolve into two, the lower-frequency band (1580—1575 cm.$^{-1}$) being assigned to primary amide II absorption, and that at 1605 cm.$^{-1}$ to skeletal " thiazole I " absorption. In the hydrazides (26—28) the strong bands between 1660 and 1645 cm.$^{-1}$ are assigned to amide I vibrations, those at 1535, 1540, and 1580 cm.$^{-1}$

[14] Bellamy, ref. 10, p. 179.
[15] Eisner and Erskine, *J.*, 1958, 971.
[16] Bellamy, ref. 10, pp. 71—72.
[17] Bellamy, ref. 10, p. 210.

See Table 1.

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to secondary amide II vibrations, and the remaining bands at 1615, 1620, and 1625 cm.$^{-1}$ to the NH deformation mode of the NH_2 group. In the thioamides (35, 36) the strong bands at 1615 and 1595 cm.$^{-1}$ respectively are likewise assigned to NH deformation vibrations.[18]

None of the simpler thiazole carboxylic acids (29—32) shows any bands in the " thiazole I " region; the carbonyl absorption occurs in the range 1695—1670 cm.$^{-1}$ with an additional strong band at 1715 cm.$^{-1}$ for thiazole-2,4-dicarboxylic acid (29). The keto-esters (37—39) similarly show no " thiazole I " bands, and the ketonic-carbonyl frequencies lie between 1695 and 1690 cm.$^{-1}$. In spectra of the keto-acids (40, 41) the acid- and ketonic-carbonyl frequencies are not resolved in the solid state, but give a single strong band at 1680 cm.$^{-1}$. The hydroxy-acids (43, 44) show acid-carbonyl absorption at 1685 and 1700 cm.$^{-1}$, respectively, but no absorption in the " thiazole I " region. In the amino-acid hydrochlorides (45—47) the acid-carbonyl frequency is at or near to 1700 cm.$^{-1}$, and the bands between 1605 and 1570 cm.$^{-1}$ are probably associated with NH_3^+ deformation frequencies, although exact assignment is difficult.

The band at 1626 cm.$^{-1}$ in Nujol falling to 1605 cm.$^{-1}$ in chloroform shown by 2-aminothiazole (48) is due to NH deformation vibrations of the amino-group. Similar bands in the range 1622—1598 cm.$^{-1}$ are observed in spectra of other 2-aminothiazoles (51, 53—56, 58). For the benzamido-derivatives (59—62) the amide I band in the solid state occurs in the region 1640—1635 cm.$^{-1}$ shifting to close to 1660 cm.$^{-1}$ in chloroform (59, 60). The two characteristic benzoyl bands near 1600 and 1580 cm.$^{-1}$ are also observed. In the solid state the secondary amide II band appears between 1520 and 1530 cm.$^{-1}$. The bands at 1595 and 1573 cm.$^{-1}$ in the sulphanilamide (74) are very probably due to a combination of NH deformation vibrations and the vibrations of the benzene ring. The exact assignment of the bands in the more complex molecules (57, 63—67) in this region has not been attempted but the bands are certainly due to NH deformation modes and vibrations of the benzene rings.

The acetamidothiazoles (68—72) in mineral oil mulls show the secondary amide I band in the range 1685—1648 cm.$^{-1}$ and the secondary amide II band between 1561 and 1542 cm^{-1}. In the tertiary amide (73) the amide I band occurs at 1648 cm.$^{-1}$; in this compound there is a weak band at 1542 cm.$^{-1}$, which could be due to a thiazole skeletal vibration.

(c) 1535—1475 cm.$^{-1}$ *region.* This includes the " thiazole II " region (1538—1493 cm.$^{-1}$) of Randall *et al.*[2] which we should certainly extend as far as 1475 cm.$^{-1}$ and possibly to 1470 cm.$^{-1}$. Thiazole (1) itself shows a very strong band at 1485 cm.$^{-1}$, and all the compounds examined possess one or two bands in this region except a small number (8, 49, 50, 52, 68—72); some of these compounds (68—72) were investigated in mineral oil mulls on an instrument of apparently low sensitivity, where bands in part of the " thiazole II " region would be masked by the absorption of the mineral oil itself. For the majority of the compounds examined one or both of the bands in this region are of medium or strong intensity, exceptions being 4-cyanothiazole (33), 2,4'-bithiazolyl-4-carbonamide (25) in the crystalline state, and 2,4'-bithiazolyl-4-carbothioamide (36).

The 1475—1350 cm.$^{-1}$ *Region* (Table 2).—This region of the spectrum includes both the CH_3 and CH_2 deformation vibrations, giving rise to absorptions near 1460 (asymmetrical mode) and 1375 cm.$^{-1}$ (symmetrical mode). Taurins, Fenyes, and Jones [3] concluded that, since thiazole (1) showed a strong band at 1385 cm.$^{-1}$, the bands at 1445 and 1435 cm.$^{-1}$ in the methylthiazoles (2—6) arose by absorption of the methyl groups, and that bands at 1385—1375 cm.$^{-1}$ are given by the thiazole skeleton as well as by the methyl groups. Most of the thiazoles examined had several bands in the 1475—1350 cm.$^{-1}$ region, and the majority possessed at least one band in the range 1445—1385 cm.$^{-1}$, usually of medium or strong intensity (exceptions being 27, 56, 68—73 where no absorption at all could be observed in the region under discussion).

[18] Bellamy, ref. 10, p. 256.

The 1350—1175 cm.$^{-1}$ *Region* (Table 2).—This is a complex region with many bands due to substituent groups, in addition to the skeletal thiazole vibrations. Thiazole (1) shows two very strong bands in this region, at 1320 and 1240 cm.$^{-1}$. All the compounds investigated, with only two exceptions (28, 70) have at least one band of usually medium to strong intensity within the range 1345—1290 cm.$^{-1}$, which includes the range 1315—1300 cm.$^{-1}$ regarded by Sheinker *et al.*[4] on the basis of their smaller selection of data as being linked with oscillations of the thiazole ring, and the majority possess a medium to strong band in the range 1250—1195 cm.$^{-1}$. Taurins *et al.*[3] assigned the bands at 1192—1175 cm.$^{-1}$ to skeletal C–CH_3 vibrations. Bands in this region occur in several compounds other than methyl derivatives, but it is of interest that a strong or medium band within the range 1190—1175 cm.$^{-1}$ is a constant feature of the 4-substituted bithiazolyls (13, 21, 22, 25, 26, 31, 34, 36) regardless of the nature of the substituent.

The 1175—930 cm.$^{-1}$ *Region* (Table 3).—(a) 1175—1050 cm.$^{-1}$ *region.* Thiazole (1) itself shows a very strong band at 1120 cm.$^{-1}$. Most of the 2-monosubstituted thiazoles examined (2, 9, 10, 48—50, 68, 74) have one main band in the range 1160—1130 cm.$^{-1}$ accompanied by a less intense band of lower frequency, at 1088—1055 cm.$^{-1}$. 2-Phenylthiazole (10) has in addition two more bands (1092w and 1053s); in 2-bromothiazole (9) the lower-frequency band is at 1047 cm.$^{-1}$, and 2-dimethylaminothiazole (50) has four bands in this region. In contrast, the 4- and 5-monosubstituted thiazoles (3, 4, 12, 24, 30, 33, 35) all have a single band between 1135 and 1090 cm.$^{-1}$, and in only one (24) is it accompanied by a lower-frequency band (at 1085 cm.$^{-1}$). Amongst the thirty-two 2,4-disubstituted thiazoles (5, 16, 17, 23, 27—29, 32, 37—47, 51, 52, 54—64, 69, 71, 73, 76) investigated, all except five have at least one band within the range 1140—1077 cm.$^{-1}$, usually of medium or strong intensity. The five exceptions (56, 69, 71, 73, 76) are all compounds whose spectra were taken from the literature, and accurate detailed values are not available. The two 2,5-disubstituted thiazoles (6, 11) had strong bands at 1160 and 1152 cm.$^{-1}$, respectively. The 2,4,5-trisubstituted thiazoles (7, 53, 65—67, 70, 72, 75) have no strong bands in this region, but since three (65—67) contain phenyl groups which show absorption in this region, and five (7, 53, 70, 72, 75) have been abstracted from the literature and are therefore of uncertain accuracy, caution must be exercised in interpreting these results. The absence of strong bands in the trisubstituted thiazoles does suggest, however, that this is the region of C–H in-plane deformation vibrations.

The ten polythiazolyls examined (13—15, 21, 22, 25, 26, 31, 34, 36) all possessed a single band, usually of medium intensity, within the range 1153—1075 cm.$^{-1}$, except (22), which showed an additional weak band at 1100 cm.$^{-1}$.

(b) 1050—930 cm.$^{-1}$ *region.* The 4-monosubstituted thiazoles (3, 12, 24, 30, 33, 35) show the most characteristic behaviour in this region, all showing a strong band in the 980—930 cm.$^{-1}$ region. The 2-monosubstituted thiazoles (2, 9, 10, 48—50, 68, 74) and the 5-monosubstituted compound (4) all show bands of widely varying frequency and intensity, while thiazole (1) itself has a single very strong band at 1040 cm.$^{-1}$. The rest of the compounds generally show one or more medium or strong bands whose frequencies do not bear any obvious relation to the pattern of substitution or nature of the substituent.

The 930—650 cm.$^{-1}$ *Region* (Table 3).—The bands in this region are usually associated with ring vibrations and C–H out-of-plane deformations. The data for certain compounds (7, 9, 49—53, 56, 57, 68—73, 75, 76), which were abstracted from the literature, are probably not complete.

(a) 930—800 cm.$^{-1}$ *region.* All the 2- and 4-monosubstituted thiazoles (2, 3, 9, 10, 12, 24, 30, 33, 35, 48—50, 68, 74) possess strong or medium bands within the range 890—850 cm.$^{-1}$. Thiazole (1) itself shows two strong bands at 880 and 860 cm.$^{-1}$, and Sheinker *et al.*[4] regard a band in the 880—860 cm.$^{-1}$ region as being perhaps characteristic of the thiazole ring. The 2,4- and 2,5-disubstituted thiazoles and the 2,4,5-trisubstituted compounds seldom exhibit bands in this range. When the substituents are thiazole rings (13—15, 21, 22, 25, 26, 31, 34, 36), however, or when there are two thiazole nuclei in close

proximity in the molecule (16, 17) a strong band in the 890—860 cm.$^{-1}$ region again appears. Of all the compounds examined, the 4-monosubstituted thiazoles (3, 12, 24, 30, 33, 35) show the greatest complexity in the 930—800 cm.$^{-1}$ region, possessing from two to four strong bands. A similar complexity is found in the polythiazolyls or in compounds where there are two thiazole nuclei close to each other in the molecule (13—17, 21, 22, 25, 26, 31, 34, 36).

(b) 800—700 cm.$^{-1}$ *region.* Thiazole (1) has two strong bands at 800 and 720 cm.$^{-1}$, and nearly all the compounds investigated possessed at least one strong or medium band in this region. The absorption pattern here appears to depend more on the nature of the substituent than on the type of substitution; for example, the simple alkyl and phenyl derivatives (2—6, 8, 10, 11) have usually a single strong band, while the simple carboxylic acids (29—32) appear to have two medium intensity bands. Similarly, closely related compounds have very similar absorption patterns (24—26, 37—39, 45—47). The absence of bands in the trisubstituted compounds (7, 53, 65—67, 70, 72), except for the absorption of the monosubstituted benzene ring, appears to suggest that absorptions in this region are attributable to C–H out-of-plane deformation modes, but this conclusion should be regarded with caution, since it is based on observations on a very limited number of compounds.

(c) 700—650 cm.$^{-1}$ *region.* As expected, all compounds containing monosubstituted benzene rings for which accurate measurements are available, show a strong (10, 11, 59—66), or medium (32), band in this region, due to the C–H out-of-plane deformation mode. In addition, three methyl derivatives (3, 5, 6) show strong to medium bands in the 670—652 cm.$^{-1}$ range. The only other compounds to show absorption in this region were all those compounds containing an NH_2 group, in the form of a primary amine, amide, thioamide (except 36), or hydrazide (23—28, 35, 45—48, 54, 55, 58, 63, 64, 74); other exceptions were compounds (65) and (66) where the band might be masked by the monosubstituted aromatic absorption, and compound (67).

These observations may be summarised as follows. The " thiazole I " band [2] in the 1625—1535 cm.$^{-1}$ region is only observed in certain thiazole derivatives, and is usually weak. This is in marked contrast to the thiazolines [7] which show intense C=N absorption in the range 1640—1550 cm.$^{-1}$. Nearly all the thiazoles investigated showed one or two medium to strong bands in the " thiazole II " region [2] (1535—1475 cm.$^{-1}$). Similarly, most of them have at least one medium to strong band in the range 1445—1385 cm.$^{-1}$. These three regions correspond to the three approximate skeletal frequencies quoted for substituted thiazoles by Katritzky [8] (1610, 1500, and 1380 cm.$^{-1}$).

Most of the thiazoles have bands in the 1345—1290 cm.$^{-1}$ and 1250—1195 cm.$^{-1}$ regions, usually strong to medium, and all the 4-substituted bithiazolyls have a medium to strong band in the 1190—1175 cm.$^{-1}$ region. Most of the 2-monosubstituted thiazoles examined had one main band in the range 1160—1130 cm.$^{-1}$, accompanied by a less intense band in the range 1088—1055 cm.$^{-1}$. In contrast, the 4- and 5-monosubstituted thiazoles had a single band in the 1135—1090 cm.$^{-1}$ region. In addition, the 4-monosubstituted compounds all had a strong band in the 980—930 cm.$^{-1}$ region, and showed a complex pattern (two to four strong bands) in the 930—800 cm.$^{-1}$ region. All the 2- and 4-monosubstituted thiazoles had strong bands in the 890—850 cm.$^{-1}$ range. The majority of the 2,4-disubstituted derivatives possessed at least one band within the range 1140—1077 cm.$^{-1}$, but seldom exhibited bands in the 890—850 cm.$^{-1}$ region; the polythiazolyls, however, all showed a strong band in this range. The trisubstituted thiazoles showed no strong bands in either the 1160—1050 cm.$^{-1}$ or the 930—800 cm.$^{-1}$ region. The only compounds to show bands between 700 and 650 cm.$^{-1}$ were those containing a monosubstituted benzene ring, some methyl derivatives, and those compounds containing an NH_2 group in the form of primary amine, amide, thioamide, or hydrazide. There appears to be no correlation between the number and position of the bands in the 930—650 cm.$^{-1}$ region and the pattern of substitution, as there is in the benzene and pyridine series.

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Experimental

All the infrared spectra were measured with a Perkin–Elmer double-beam recording spectrophotometer (model 21) incorporating a sodium chloride prism.

Dimethyl 2,2′-Methylenebisthiazole-4,4′-dicarboxylate (16).—(i) A mixture of malononitrile (3·3 g.), liquid hydrogen sulphide (*ca.* 3 c.c.), and triethanolamine (3 drops) in ethanol (20 c.c.) was heated at 50° in a sealed tube for 6 hr. The crystalline product (6·35 g., 95%) was collected, washed with ethanol, and dried at 100°. Recrystallisation from dimethylformamide–ethanol gave dithiomalonamide as yellow needles, m. p. 214—215° (decomp.). Lehr, Guex, and Erlenmeyer [19] report m. p. 212° (decomp.).

(ii) The preceding product (1·34 g.) was heated on a water-bath with methyl bromopyruvate (3·62 g.) and dimethylformamide (5 c.c.) for 2 hr. The brown crystals which separated on cooling were collected, washed with ethanol, and dried at 100°. Recrystallisation from dimethylformamide–ethanol gave *dimethyl 2,2′-methylenebisthiazole-4,4′-dicarboxylate* (850 mg., 30%) as pale yellow plates, m. p. 177—179° (Found: C, 44·6; H, 3·5; N, 9·3. $C_{11}H_{10}N_2O_4S_2$ requires C, 44·3; H, 3·4; N, 9·4%).

Dimethyl 2,2′-p-Phenylenebisthiazole-4,4′-dicarboxylate (17).—(i) A mixture of terephthalonitrile [20] (750 mg.), liquid hydrogen sulphide (*ca.* 2 c.c.), triethanolamine (2 drops), and ethanol (20 c.c.) was heated at 50° in a sealed tube for 6 hr. The crystalline product was collected and washed with a little ethanol. Recrystallisation from dimethylformamide–ether gave dithioterephthalamide as yellow plates (870 mg., 76%), m. p. 271—273°. Luckenbach [21] reports m. p. 263° (decomp.).

(ii) A mixture of the preceding compound (392 mg.) and methyl bromopyruvate (724 mg.) in dimethylformamide (5 c.c.) was heated at 100° for 2 hr. After cooling, the product was collected and recrystallised from dimethylformamide, giving *dimethyl 2,2′-p-phenylenebisthiazole-4,4′-dicarboxylate* (440 mg., 61%) as off-white crystals, m. p. 253—256° (Found: C, 53·5; H, 3·3; N, 7·8. $C_{16}H_{12}N_2O_4S_2$ requires C, 53·3; H, 3·3; N, 7·8%).

2,4′-Bithiazolyl-4-carbohydrazide (26).—A mixture of ethyl 2,4′-bithiazolyl-4-carboxylate (544 mg.) and hydrazine hydrate (110 mg.) in ethanol (7 c.c.) was heated under reflux for 2 hr. After cooling, the crystalline product was collected and recrystallised from dimethylformamide–ethanol, giving the *hydrazide* (450 mg., 88%) as colourless needles, m. p. 264—266° (Found: C, 37·6; H, 2·9; N, 24·4. $C_7H_6N_4OS_2$ requires C, 37·1; H, 2·7; N, 24·7%).

2-Aminothiazole-4-carbohydrazide (27).—A mixture of ethyl 2-aminothiazole-4-carboxylate [22] (1·72 g.) and hydrazine hydrate (1·0 g.) in ethanol (10 c.c.) was heated under reflux for 1 hr. The solution was filtered, and the crystals which separated on cooling were collected. Recrystallisation from ethanol gave *2-aminothiazole-4-carbohydrazide* (1·5 g., 95%) as colourless needles, m. p. 192—195° (Found: C, 30·6; H, 3·7; S, 20·1. $C_4H_6N_4OS$ requires C, 30·4; H, 3·8; S, 20·3%).

2-Hydrazinothiazole-4-carbohydrazide (28).—Ethyl 2-bromothiazole-4-carboxylate (600 mg.) was heated under reflux with hydrazine hydrate (590 mg.) in ethanol (10 c.c.) for 1 hr. The crystalline *product*, which separated on cooling, was collected, and crystallised from dimethylformamide–ethanol as fawn needles (170 mg., 39%), m. p. 235—236° (decomp.) (Found: C, 28·0; H, 4·4; S, 18·2. $C_4H_7N_5OS$ requires C, 27·7; H, 4·1; S, 18·5%).

2,4′-Bithiazolyl-4-carboxylic Acid (31).—Ethanolic 10% potassium hydroxide (20 c.c.) was added to a suspension of methyl 2,4′-bithiazolyl-4-carboxylate (2·26 g.) in ethanol (50 c.c.), and the mixture warmed on a water-bath for 10 min. The ester dissolved and the potassium salt of the acid was precipitated. The salt was dissolved in water (35 c.c.), and the solution acidified to Congo Red with concentrated hydrochloric acid. Evaporation to dryness and recrystallisation of the residue from 20% aqueous acetic acid gave *2,4′-bithiazolyl-4-carboxylic acid* (1·94 g., 91%) as colourless needles, m. p. 231—232° (Found: C, 39·6; H, 1·9; N, 12·9. $C_7H_4N_2O_2S_2$ requires C, 39·6; H, 1·9; N, 13·2%).

2-1′-Benzamidoethyl-4-benzylthiazole (61).—A mixture of α-benzamidopropionothioamide [23] (1·04 g.) and benzyl chloromethyl ketone (842 mg.) in methanol (10 c.c.) was heated under

[19] Lehr, Guex, and Erlenmeyer, *Helv. Chim. Acta*, 1944, **27**, 971.
[20] Rouiller, *Amer. Chem. J.*, 1912, **47**, 475.
[21] Luckenbach, *Ber.*, 1884, **17**, 1430.
[22] Steude, *Annalen*, 1891, **261**, 26.
[23] Goldberg and Kelly, *J.*, 1947, 1372.

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reflux for 4 hr. The methanol was removed by distillation, and the residual oil taken up in benzene and washed with aqueous sodium carbonate and water. Removal of the benzene left an oil (1·5 g., 93%) which slowly crystallised. Recrystallisation from aqueous ethanol (charcoal) gave 2-1′-*benzamidoethyl*-4-*benzylthiazole* as colourless needles, m. p. 127—129° (Found: C, 70·2: H, 5·8; N, 8·6. $C_{19}H_{18}N_2OS$ requires C, 70·8; H, 5·6; N, 8·7%).

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660. *Chemistry of Micrococcin* P. *Part VI.* Racemisation of 2-(1-Amino-2-methylpropyl)thiazole-4-carboxylic Acid, and Related Studies.*

By (Mrs.) B. M. Dean, (Mrs.) M. P. V. Mijović, and James Walker.

Optically active 2-(1-amino-2-methylpropyl)- (I; R = Pr^i) and 2-1′-aminoethyl-thiazole-4-carboxylic acid (I; R = Me) readily undergo racemisation, although the corresponding 2-(1-amino-2-methylpropyl)- (IV; R = Pr^i) and 2-1′-aminoethyl-4-phenylthiazole (IV; R = Me) appear to be optically stable. 2-(1-Amino-2-methylpropyl)thiazole-4-carboxylic acid (I; R = Pr^i) as incorporated into micrococcin *P* is probably of the D-configuration.†

In Part I,[1] it was reported that the amino-acid, 2-(1-amino-2-methylpropyl)thiazole-4-carboxylic acid (I; R = Pr^i), had been isolated in an optically active form as its hydrochloride from the products obtained by the hydrolysis of the antibiotic micrococcin *P* with hot 20% hydrochloric acid. Micrococcin *P* appears to be derived biogenetically from a cysteine-rich peptide,[1,2] and it therefore seemed appropriate to investigate the optical form of the amino-acid (I; R = Pr^i), as the less common D-forms of the natural amino-acids are frequently found incorporated into polypeptide antibiotics.[3] The amino-acid (I; R = Pr^i) can be regarded as being derived from a valyl-cysteinyl residue in the hypothetical precursor[1,2] of micrococcin *P* and the obvious course was to relate the amino-acid (I; R = Pr^i) with natural L-valine.

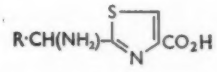
We have previously[4] described the synthesis of DL-2-(1-amino-2-methylpropyl)-thiazole-4-carboxylic acid (I; R = Pr^i) from DL-valine, and the same synthetic methods were therefore applied to L-valine. Benzoylation, esterification with diazomethane, and treatment with methanolic ammonia gave L-α-benzamido-β-methylbutyramide. Dehydration of the latter with phosphoryl chloride in pyridine[5] gave the nitrile, which was converted into the thioamide by the addition of hydrogen sulphide. Benzenesulphonyl chloride and pyridine,[6] which have been commended for use with optically active amides,[7] were used in the DL-series[4] but offered, in this case, no advantage over phosphoryl chloride and pyridine in the preparation of the optically active nitrile. In fact the use of benzenesulphonyl chloride and pyridine resulted in poor conversion at room temperature and considerable racemisation of the resulting nitrile at water-bath temperature. Optical activity was well retained throughout these operations involving reaction at the carbon

* Part V, preceding communication.

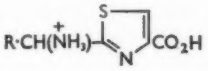
† L- and D- in such cases in this paper refer to the configuration of the α-amino-acid from which the side-chain and $C_{(2)}$ of the ring may be considered to be derived or are in fact derived.

[1] Brookes, Fuller, and Walker, *J.*, 1957, 689.
[2] Brookes, Clark, Fuller, Mijović, and Walker, *J.*, 1960, 916.
[3] Cf. Arnstein, *Ann. Reports*, 1957, **54**, 347; Abraham and Newton, Proc. IVth Internat. Congress Biochem. (Vienna), 1959, **5**, 50.
[4] Brookes, Clark, Majhofer, Mijović, and Walker, *J.*, 1960, 925.
[5] Delaby, Tsatsas, and Lusinchi, *Compt. rend.*, 1956, **242**, 2644.
[6] Stephens, Bianco, and Pilgrim, *J. Amer. Chem. Soc.*, 1955, **77**, 1701.
[7] Peterson and Niemann, *J. Amer. Chem. Soc.*, 1957, **79**, 1389.

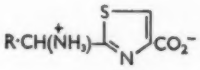
atom adjacent to the asymmetric centre; the optical rotation showed a reversal of sign at each stage. Condensation of the L-thioamide with ethyl bromopyruvate gave ethyl L-2-(1-benzamido-2-methylpropyl)thiazole-4-carboxylate with a relatively low, but quite definite, specific rotation. When this product was hydrolysed with acid the resulting L-2-(1-amino-2-methylpropyl)thiazole-4-carboxylic acid (I; R = Pr^i) hydrochloride appeared to have a small dextrorotation, differing significantly numerically from the figure (15·3° at *c* 0·69 in water) recorded [1] for the substance isolated from the hydrolysis products of micrococcin *P*. Sufficient material from the earlier isolation remained for a determination of the optical rotation of the amino-acid hydrochloride from the hydrolysis of micrococcin *P*, and it was comparable in magnitude but of opposite sign to that of the substance obtained by synthesis from L-valine at the concentration (*c* 2·5 in water) studied. Two further isolations of the amino-acid hydrochloride from hydrolyses of micrococcin *P* were then undertaken. In the first of these the product showed a lævorotation in one observation and no perceptible rotation in two others at different concentrations. In the second isolation the product showed lævorotations in three different observations; when two solutions were further examined after an interval, no perceptible rotations were observed. A further preparation of the synthetic product was therefore undertaken and pure recrystallised ethyl L-2-(1-benzamido-2-methylpropyl)thiazole-4-carboxylate was hydrolysed as before, but, in this case, the resulting amino-acid hydrochloride showed no perceptible rotation. We were therefore obliged to conclude that the amino-acid (I; R = Pr^i) undergoes ready racemisation. The fact that it seemed to survive lengthy treatment in strongly acid media without complete racemisation suggests that the cation (II; R = Pr^i) is reasonably stable, and that it is the dipolar ion (III; R = Pr^i) that is stereochemically labile. Lack of material has, however, prevented a more detailed study. Lævorotations * have been observed repeatedly for material isolated from micrococcin *P*, and, as material synthesised from L-valine has shown a dextrorotation, the amino-acid (I; R = Pr^i) incorporated in micrococcin *P* is apparently related configurationally to D-valine.



(I)



(II)



(III)

In the hope of throwing light on this loss of optical activity a similar series of experiments was carried out starting from L-alanine, and, although optical activity was retained throughout the series of intermediates, the final product, 2-1′-aminoethylthiazole-4-carboxylic acid (I; R = Me) hydrochloride, showed no perceptible rotation.

Further experiments were carried out with the object of studying the effects of a 4-substituent other than the carboxyl group on the optical properties of a 2-1′-aminoalkylthiazole. For this purpose D-α-benzamido-β-methylbutyrothioamide and L-α-benzamidopropionothioamide were severally condensed with ω-bromoacetophenone in alcoholic solution in presence of calcium carbonate. Hydrolysis of the products afforded D-2-(1-amino-2-methylpropyl)-4-phenylthiazole (IV; R = Pr^i) and L-2-1′-aminoethyl-4-phenylthiazole (IV; R = Me) hydrochlorides which appeared to be optically stable. However, condensation of L-α-benzamidopropionothioamide and ω-bromoacetophenone in presence of pyridine gave racemic 2-1′-benzamidoethyl-4-phenylthiazole.

These experiments suggest that the apparently ready racemisations of the acids (I; R = Pr^i and Me) are related to the presence of the 4-carboxyl group. Our observations are also in line with the fact that thiostreptoic acid (V), liberated from the antibiotic thiostrepton by acid hydrolysis, also appears to be optically inactive,[8] although the latter

* The sign of rotation recorded previously [1] appears to have been incorrect.

[8] Bodanszky, Sheehan, Fried, Williams, and Birkhimer, *J. Amer. Chem. Soc.*, 1960, **82**, 4747.

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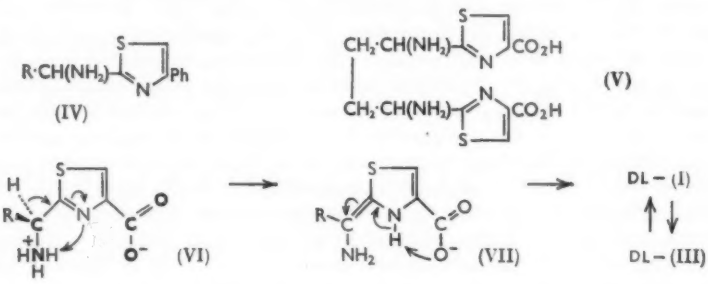
could be either a racemate or a *meso*-form. Inspection of a model of 2-(1-amino-2-methylpropyl)thiazole-4-carboxylic acid shows that in the related dipolar ion the preferred conformation should be that (VI; R = Pr^i) in which the atoms shown bold lie in the same



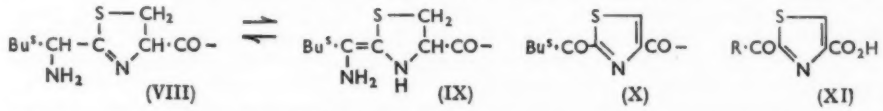
plane as the thiazole ring, and the transfer of a proton from the exocyclic ammonio-group to the ionised carboxyl group might be facilitated by participation of the ring-nitrogen atom as an intermediate " relay station " (VII) in a concerted process involving loss of asymmetry at the asymmetric centre.

Parallel optical behaviour is seen in the thiazoline antibiotic bacitracin A, in which the corresponding asymmetric centre in the terminal 2-(1-amino-2-methylbutyl)thiazolinyl-4-carbonyl residue [9] (VIII) shows similar lability. This portion of the bacitracin A molecule is derived biogenetically from a *N*-terminal L-isoleucyl-L-cysteinyl fragment of a peptide chain and gives rise on acid hydrolysis to L-cysteine and L-isoleucine, accompanied, however, by 0·5 mole of D-alloisoleucine per mole of bacitracin A; [10,11] it has also been proved [11] that it is this terminal L-isoleucyl residue which is concerned in the formation of the alloisoleucine and neither of the other two L-isoleucyl residues in the antibiotic. The stereochemical lability of this asymmetric centre in bacitracin A has been interpreted [11 12] in terms of tautomeric interconversion between the forms (VIII) $\rightleftharpoons$ (IX), and it has more recently been shown [12] that stereochemical equilibration in this instance can take place in the intact antibiotic in 3% acetic acid at room temperature in a few days and in solution at pH 4·52 at 4° in the course of a month. The situation in bacitracin A, however, is further complicated by lack of precise knowledge of the interaction that appears to exist between this area of the molecule and the phenylalanine residue.

Besides showing stereochemical instability the same positions in bacitracin A and in 2-(1-amino-2-methylpropyl)thiazole-4-carboxylic acid (I; R = Pr^i) are involved in remarkably ready oxidative loss of ammonia with generation of carbonyl groups. Thus, bacitracin A is changed by exposure in solution at pH 7 or slightly higher into bacitracin F in which the terminal substituted thiazoline group (VIII) is replaced by the corresponding 2-acylthiazolyl-4-carbonyl group (X) with loss of ammonia and conversion of the thiazoline ring into a thiazole structure; [13] and 2-(1-amino-2-methylpropyl)thiazole-4-carboxylic acid (I; R = Pr^i) is converted with very great ease at room temperature into 2-isobutyryl-thiazole-4-carboxylic acid (XI; R = Pr^i) by treatment with dilute alkaline potassium permanganate solution,[1] a process which similarly converts thiostreptoic acid (V) into the related 2,2′-succinoylbisthiazole-4,4′-dicarboxylic acid.[8] In view of the probable mode of biosynthesis of micrococcin *P* discussed previously [1,2,4] in this series of papers, it is likely

[9] Hausmann, Weisiger, and Craig, *J. Amer. Chem. Soc.*, 1955, **77**, 721.
[10] Craig, Hausmann, and Weisiger, *J. Amer. Chem. Soc.*, 1954, **76**, 2839.
[11] Lockhart, Abraham, and Newton, *Biochem. J.*, 1955, **61**, 534.
[12] Konigsberg and Craig, *J. Amer. Chem. Soc.*, 1959, **81**, 3452.
[13] Hausmann, Weisiger, and Craig, *J. Amer. Chem. Soc.*, 1955, **77**, 730; Weisiger, Hausmann, and Craig, *ibid.*, p. 3123.

that oxidative loss of ammonia at some stage accounts for the appearance of 2-propionylthiazole-4-carboxylic acid (XI; R = Et) among the hydrolytic products from micrococcin *P* rather than 2-1′-aminopropylthiazole-4-carboxylic acid (I; R = Et), although it is not yet possible to say whether 2-propionyl- (XI; R = Et) and 2-(1-amino-2-methylpropyl)-thiazole-4-carboxylic acid (I; R = Pr^{i}) " may be incorporated in micrococcin *P* in the form in which they are isolated after hydrolysis, or the appearance of one as the



(VIII) (IX) (X) (XI)

ketonic and the other as the amino-derivative may be related to the position occupied in the molecule of the antibiotic and to the order of events during hydrolysis." [1] It is of interest that in one laboratory [14] 2-1′-aminopropylthiazole-4-carboxylic acid (I; R = Et) has been obtained on acid hydrolysis of thiostrepton, and a report from another group [8] describes the isolation after similar treatment of thiostrepton of the related keto-acid (XI; R = Et), identical with the fragment isolated from micrococcin *P*,[1] in addition to the amino-acid (I; R = Et). Another theory for the mode of origin of 2-propionylthiazole-4-carboxylic acid (XI; R = Et) in the hydrolysis of micrococcin *P* has been proposed,[14] based on the incorporation of the threonine analogue [I; R = Me·CH(OH)·] into the antibiotic, but is considered unlikely in view of the appearance of α-aminobutyric acid among the products formed by treatment of micrococcin *P* with sodium and liquid ammonia followed by acid hydrolysis.[4]

Micrococcin *P* was the first antibiotic reported [1] to contain thiazole structures showing a definite pattern relating them to cysteine peptide precursors and it is of interest that a similar pattern has emerged from the antibiotics thiostrepton [8,14] and bottromycin.[15]

Experimental

L-Valine and L-alanine were commercial specimens of satisfactory purity (specific rotation and paper chromatography); D-valine, kindly supplied by Dr. D. F. Elliott, had been obtained by resolution of DL-valine.[16]

L-α-*Benzamido*-β-*methylbutyramide*.—(i) L-Valine was benzoylated by the usual Schotten–Baumann method, and the product, after crystallisation from water, had m. p. 113—115°, $[\alpha]_D^{21}$ +22·0° (*c* 4·9 in 95% ethanol); Fox *et al.*[17] record m. p. 131—132° and $[\alpha]_D^{25}$ +21·8° (*c* 4·9 in 95% ethanol). Our lower m. p. may be due to dimorphism, as the m. p. of the D-derivative agreed with that recorded by Fox *et al.* for the L-compound.

(ii) Treatment of the preceding product with ethereal diazomethane afforded *N*-benzoyl-L-valine methyl ester, which crystallised from aqueous methanol as needles, m. p. 113—114°, $[\alpha]_D^{21}$ −8·0° (*c* 5 in methanol); Reihlen and Knöpfle [18] record m. p. 110·5° and $[M]_D$ −18° (*i.e.*, $[\alpha]_D$ −7·7°) (*c* 0·4 in methanol). The D-compound had m. p. 111° and $[\alpha]_D^{24}$ +8·2° (*c* 5 in methanol).

(iii) The preceding ester (4·12 g.) was heated at 110° for 8 hr. in a small stainless-steel bomb with methanol (40 c.c.), which had been saturated with ammonia at 0°. After cooling, the crystalline product (2·23 g., 58%) was collected and washed with ether. The material obtained by evaporation of the combined ether washings and mother-liquors could be re-cycled with methanolic ammonia. Recrystallisation from aqueous methanol gave L-α-*benzamido*-β-*methylbutyramide* as prismatic needles, m. p. 242—244°, $[\alpha]_D^{21}$ +50·3° (*c* 2·5 in dimethylformamide); a sample was sublimed at 215°/15 mm. for analysis (Found: C, 65·4; H, 7·1; N, 12·6. $C_{12}H_{16}N_2O_2$ requires C, 65·4; H, 7·3; N, 12·7%). Fox *et al.*[17] quote m. p. 220—221° for the DL-compound. The D-derivative had m. p. 242°.

[14] Kenner, Sheppard, and Stehr, *Tetrahedron Letters*, 1960, No. 1, 23.
[15] Waisvisz, van der Hoeven, and te Nijenhuis, *J. Amer. Chem. Soc.*, 1957, **79**, 4524.
[16] Birnbaum, Levintow, Kingsley, and Greenstein, *J. Biol. Chem.*, 1952, **194**, 455.
[17] Fox, Pettinga, Halverson, and Wax, *Arch. Biochem.*, 1950, **25**, 21.
[18] Reihlen and Knöpfle, *Annalen*, 1936, **523**, 199.

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L-α-*Benzamido*-β-*methylbutyrothioamide*.—(i) Redistilled phosphoryl chloride (0·75 c.c.) was added slowly with ice-cooling to the amide (1·5 g.) in dry pyridine (7·5 c.c.). After ½ hr. at room temperature, the mixture was poured on ice. The aqueous solution was extracted with ether, and the extract was washed with dilute hydrochloric acid and water, dried, and evaporated. The oily nitrile (1·0 g., 72%) rapidly crystallised, and then separated from benzene in prisms, m. p. 118—120°, $[\alpha]_D^{21}$ −52·0° (*c* 1·25 in 95% ethanol). The D-derivative had $[\alpha]_D^{21}$ +52·8° (*c* 1·25 in 95% ethanol).

(ii) The preceding nitrile (600 mg.) was added to liquid hydrogen sulphide (*ca.* 2 c.c.) followed by cold (−80°) ethanol (2 c.c.) containing triethanolamine (50 mg.), and the mixture was heated at 55° for 8 hr. in the manner previously described.[4] The L-*thioamide* crystallised from ethanol as almost colourless needles (620 mg., 89%), m. p. 178—185°; an analytical specimen had m. p. 185—192°, $[\alpha]_D^{24}$ +86·6° (*c* 2·5 in dimethylformamide) (Found: C, 60·9; H, 6·8; N, 11·6. $C_{13}H_{16}N_2OS$ requires C, 61·0; H, 6·8; N, 11·9%). The D-thioamide had m. p. 185°, $[\alpha]_D^{21}$ −85·6° (*c* 2·5 in dimethylformamide).

Ethyl L-2-(1-*Benzamido*-2-*methylpropyl*)*thiazole*-4-*carboxylate*.—The preceding thioamide (400 mg.) was heated under reflux with ethyl bromopyruvate (340 mg.) in ethanol (6 c.c.) for 2 hr. The solvent was removed under reduced pressure, and the residue was taken up in benzene and washed with aqueous sodium carbonate and water. Evaporation of the benzene left a pale yellow oil (540 mg., 96%), which crystallised when rubbed with ethyl acetate. Recrystallisation from aqueous ethanol gave *ethyl* L-2-(1-*benzamido*-2-*methylpropyl*)*thiazole*-4-*carboxylate* as colourless needles, m. p. 119—120°, $[\alpha]_D^{20}$ −3·7° (*c* 2·5 in 95% ethanol) (Found: C, 61·7; H, 6·3; N, 8·2. $C_{17}H_{20}N_2O_3S$ requires C, 61·4; H, 6·1; N, 8·4%).

Partially Racemised, and Racemised, L-2-(1-*Amino*-2-*methylpropyl*)*thiazole*-4-*carboxylic Acid* (I; R = Pr^i) *Hydrochloride*.—(*A*) The previous experiment was repeated, and the crude product was heated under reflux with 20% w/v hydrochloric acid (20 c.c.) for 4 hr. After cooling and ether-extraction to remove benzoic acid, the acid solution was evaporated to dryness. Recrystallisation of the residue from methanol–ethyl acetate (charcoal) gave prismatic needles (300 mg., 75%), m. p. 268—270° (decomp.). Further recrystallisation raised the m. p. to 272° (decomp.), essentially the same as that (269—272°) recorded for the DL-compound [4] (Found: C, 40·7; H, 5·6; N, 11·6. $C_8H_{12}N_2O_2S$,HCl requires C, 40·4; H, 5·5; N, 11·8%). Specific rotations, observed immediately after preparation of the respective solutions, were low but definitely positive, namely, $[\alpha]_D^{21}$ +2·1° (*c* 2·5 in water), $[\alpha]_D^{25}$ +5·2° (*c* 0·5 in water). At this stage there was no reason for expecting anomalous behaviour and later observations on these two solutions were not made. In view of the satisfactory analysis and paper chromatographic examination, contamination with L-(+)-valine is excluded as an explanation of the observed rotations.

(*B*) Recrystallised ethyl L-2-(1-benzamido-2-methylpropyl)thiazole-4-carboxylate (180 mg.) was heated under reflux with 20% hydrochloric acid (10 c.c.) for 4 hr. The benzoic acid was removed by ether-extraction and the aqueous layer was evaporated to dryness, leaving a colourless crystalline residue (135 mg.). This crystallised from methanol–ethyl acetate as colourless prisms (90 mg.), m. p. 259—261° (decomp.), $[\alpha]_D^{22}$ 0° (*c* 2·0 in water).

Variable Specific Rotations observed for 2-(1-*Amino*-2-*methylpropyl*)*thiazole*-4-*carboxylic Acid* (I; R = Pr^i) *Hydrochloride* (a) *Derived from Micrococcin* P, *and* (b) *Synthesised from* L-*Valine*.—Three isolations of the amino-acid hydrochloride have been made from hydrolyses of micrococcin *P* in the manner already described,[1] and the preparations are denoted (i)—(iii). Optical

Specific rotations observed for 2-(1-*amino*-2-*methylpropyl*)*thiazole*-4-*carboxylic acid hydrochloride.*

	Derived from micrococcin *P*				Synthesised from L-valine	
c	(i)	(ii)	(iii)		(i)	(ii)
0·5		−20·8°	−6·2°		+5·2°	
0·69			−12·8°	0° (next day)		
1·25		0				
2·0						0°
2·5	−2·9°	0	−2·1°	0° (in 4 hr.)	+2·1°	

rotations were observed in distilled water at the concentrations shown in the Table. Precautions were taken to ensure thermal equilibrium of solvent and apparatus in the room in which observations were made before the preparation of solutions.

L-α-*Benzamidopropionitrile*.—(i) L-Alanine was benzoylated in the usual way; the product, recrystallised from aqueous methanol, had m. p. 145—147°, $[\alpha]_D^{26}$ +36·6° (*c* 2·5 in 1·5N-potassium hydroxide); Pacsu and Mullen [19] record m. p. 148°, $[\alpha]_D^{20}$ +37·1° (*c* 6·7 neutralised with potassium hydroxide).

(ii) The methyl ester (13·3 g.), prepared with the aid of diazomethane in the usual way, was heated at 100—110° for 7 hr. in an autoclave with methanol (250 c.c.) saturated with ammonia at 0°. The amide separated from aqueous methanol in colourless needles (10·4 g.), m. p. 238—242°, $[\alpha]_D^{20}$ +43·1° (*c* 2·5 in 98% formic acid); Freudenberg and Rhino [20] record m. p. 228—229°, $[\alpha]_{578}^{21}$ +42·2° (*c* 4·9 in formic acid).

(iii) Redistilled phosphoryl chloride (0·92 c.c.) was added slowly with ice-cooling to the preceding amide (1·92 g.) in dry pyridine (7 c.c.) during 15 min. with shaking. After 30 min. at room temperature the mixture was diluted with water (100 c.c.) and extracted with ether. Unchanged amide (0·73 g.) remained undissolved and was collected. Crystallisation from benzene of the residue obtained from the ethereal solution afforded the *nitrile* as colourless prisms (0·27 g.), m. p. 125—127°, $[\alpha]_D^{22}$ −49·3° to −58·1° (*c* 2·5 in 95% ethanol) (Found: C, 68·9; H, 5·7; N, 16·1. $C_{10}H_{10}N_2O$ requires C, 68·8; H, 5·8; N, 16·2%). This preparation had to be repeated a number of times and some variation in specific rotation was observed, indicating slight racemisation and loss of optical purity. The use of toluene-*p*-sulphonyl chloride and pyridine gave better conversion at the temperature of the water-bath but a less optically pure product.

L-α-*Benzamidopropionothioamide*.—The preceding nitrile (1·15 g.) was allowed to react with liquid hydrogen sulphide (*ca.* 5 c.c.) in methanol (16 c.c.) containing triethanolamine (2 drops) at 50—60° for 6 hr. in the usual manner. The L-*thioamide* crystallised from water in prisms (1·25 g.), m. p. 155—156°, $[\alpha]_D^{20}$ +126·5° (*c* 1·25 in dimethylformamide) (Found: C, 57·3; H, 5·7; N, 13·0. $C_{10}H_{12}N_2OS$ requires C, 57·7; H, 5·8; N, 13·4%).

Ethyl L-2-1′-*Benzamidoethylthiazole*-4-*carboxylate*.—A solution of the preceding thioamide (1·04 g.) and ethyl bromopyruvate (0·99 g.) in ethanol (12 c.c.) was boiled under reflux for 2 hr., and the mixture was worked up in the manner described above for the analogous reaction. *Ethyl* L-2-1′-*benzamidoethylthiazole*-4-*carboxylate* crystallised from aqueous ethanol in colourless flattened needles (0·9 g.), m. p. 124°, $[\alpha]_D^{21}$ +9·4° (*c* 2·5 in methanol) (Found: C, 58·9; H, 5·1; N, 8·7. $C_{15}H_{16}N_2O_3S$ requires C, 59·2; H, 5·3; N, 9·2%).

The ester (700 mg.) was heated under reflux with 20% hydrochloric acid (15 c.c.) for 4 hr. Benzoic acid was extracted with ether and the aqueous phase was taken to dryness. The residue crystallised from methanol–ethyl acetate; the resulting 2-1′-aminoethylthiazole-4-carboxylic acid hydrochloride (0·4 g.) showed no perceptible optical activity (*c* 2·5 in water).

D-2-(1-*Benzamido*-2-*methylpropyl*)-4-*phenylthiazole*.—A mixture of D-α-benzamido-β-methylbutyrothioamide (470 mg.) and ω-bromoacetophenone (400 mg.) in methanol (3 c.c.) was heated under reflux in presence of powdered calcium carbonate (200 mg.) for 2½ hr. The solution was diluted somewhat with hot methanol, filtered, and concentrated. The *product* crystallised from aqueous methanol in colourless needles (350 mg.), m. p. 126°, $[\alpha]_D^{22}$ −35·5° (*c* 2·5 in dimethylformamide) (Found: C, 71·3; H, 6·0; N, 8·2. $C_{20}H_{20}N_2OS$ requires C, 71·4; H, 6·0; N, 8·3%).

D-2-(1-*Amino*-2-*methylpropyl*)-4-*phenylthiazole* (IV; R = Pr^i) *Hydrochloride*.—The preceding substance (350 mg.) was heated on the water-bath for 3½ hr. with 20% hydrochloric acid (10 c.c.). The aqueous phase was extracted with ether and taken to dryness. The residue was taken up in water and basified, and the amine was extracted with ether. The ethereal solution was dried ($MgSO_4$), concentrated, and saturated with hydrogen chloride. Solvent and excess of hydrogen chloride were removed under reduced pressure and the residue was crystallised from methanol–ethyl acetate, giving D-2-(1-*amino*-2-*methylpropyl*)-4-*phenylthiazole hydrochloride* as colourless plates (190 mg.), m. p. 201—202°, $[\alpha]_D^{22}$ −7·7° (*c* 2·14 in water) unchanged after 72 hr. (Found: C, 57·8; H, 6·2; N, 10·4. $C_{13}H_{16}N_2S$,HCl requires C, 58·1; H, 6·4; N, 10·4%). A solution in 0·08N-ethanolic potassium hydroxide showed $[\alpha]_D^{24}$ +23·8° (*c* 1·7), unchanged after 24 hr.; when this solution was evaporated to dryness with as little mechanical loss as possible with 8% ethanolic hydrogen chloride, the residue then had $[\alpha]_D^{22}$ −5·9° in water (calc. with reference to initial weight of substance).

L-2-1′-*Benzamidoethyl*-4-*phenylthiazole*.—(*A*) A mixture of L-α-benzamidopropionothioamide

[19] Pacsu and Mullen, *J. Biol. Chem.*, 1940, **136**, 335.
[20] Freudenberg and Rhino, *Ber.*, 1924, **57**, 1547.

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(300 mg.), ω-bromoacetophenone (280 mg.), and pyridine (0·2 c.c.) in methanol was boiled under reflux for 2 hr. When the solution was concentrated to small bulk the product crystallised. Recrystallisation from aqueous methanol afforded needles (0·29 g.) of racemic 2-1′-*benzamidoethyl*-4-*phenylthiazole*, m. p. 162—164°, $[\alpha]_D^{25}$ 0° (*c* 1·25 in chloroform) (Found: C, 70·0; H, 5·3; N, 8·8. $C_{18}H_{16}N_2OS$ requires C, 70·1; H, 5·2; N, 9·1%).

(*B*) The L-thioamide (300 mg.), ω-bromoacetophenone (280 mg.), and powdered calcium carbonate (200 mg.) in methanol were similarly boiled under reflux for 2 hr. Recrystallisation of the product from aqueous methanol gave colourless needles (0·46 g.) of L-2-1′-*benzamidoethyl*-4-*phenylthiazole*, m. p. 136—138°, $[\alpha]_D^{22}$ +38·7° (*c* 2·5 in dimethylformamide) (Found: C, 69·9; H, 5·4; N, 8·7; S, 10·2. $C_{18}H_{16}N_2OS$ requires C, 70·1; H, 5·2; N, 9·1; S, 10·4%).

(*C*) Partially racemised L-thioamide (416 mg., $[\alpha]_D^{23}$ +78·6°) was condensed with ω-bromoacetophenone (398 mg.) as described in (*B*) (above). Crystallisation from aqueous methanol afforded, as successive fractions, (i) racemic material (230 mg.), m. p. 161—163°, $[\alpha]_D^{22}$ 0°, identical with the substance isolated as in (*A*) (above), and (ii) the L-derivative (200 mg.), m. p. 138—140°, $[\alpha]_D^{22}$ +34·3° (*c* 2·3 in dimethylformamide).

L-2-1′-*Aminoethyl*-4-*phenylthiazole* (IV; R = Me) *Hydrochloride*.—L-2-1′-Benzamidoethyl-4-phenylthiazole (300 mg.) was hydrolysed with hot 20% hydrochloric acid (10 c.c.) in the usual way (4½ hr.). The crude product was taken up in water and basified, and the amine was recovered in ether and converted into the hydrochloride in the manner described above. L-2-1′-*Aminoethyl*-4-*phenylthiazole hydrochloride* crystallised from methanol–ethyl acetate in needles (120 mg.), m. p. 225—226°, $[\alpha]_D^{25}$ +11·4° (*c* 2·0 in water) (Found: C, 54·6; H, 5·3; S, 13·6. $C_{11}H_{12}N_2S,HCl$ requires C, 54·9; H, 5·4; S, 13·3%). A solution in 0·08N-ethanolic potassium hydroxide showed $[\alpha]_D^{25}$ −10·9° (*c* 1·0), unchanged after 24 hr.; when this solution was taken to dryness with 8% ethanolic hydrogen chloride, with as little mechanical loss as possible, the residue then had $[\alpha]_D^{24}$ +8·6° in water (calc. with reference to initial weight of substance).

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661. *The Formation of Aromatic Hydrocarbons at High Temperatures. Part XII.* The Pyrolysis of Benzene.*

By G. M. BADGER and J. NOVOTNY.

Pyrolysis of benzene at 700° has been shown to yield biphenyl as the major product, with significant amounts of *p*-terphenyl, *m*-terphenyl, and triphenylene. Fluorene, phenanthrene, anthracene, *o*-terphenyl (?), fluoranthene, chrysene, and 3,4-benzofluoranthene were also detected, and methane and ethylene were identified in the exit gases.

TARS produced by the pyrolysis of acetylene,[1] butadiene,[2] alkylbenzenes,[3] 1-phenylbuta-1,3-diene,[4] styrene,[5] indene,[6] and tetralin [7] have all been shown to contain significant quantities of benzene. It therefore seemed to be important to determine to what extent this hydrocarbon undergoes pyrolytic conversion into polycyclic compounds. Previous

* Part XI, *J.*, 1960, 4431.

[1] Badger, Lewis, and Napier, *J.*, 1960, 2825.
[2] Badger and Spotswood, *J.*, 1960, 4431.
[3] Badger and Spotswood, *J.*, 1960, 4420.
[4] Badger and Spotswood, *J.*, 1959, 1635.
[5] Badger and Buttery, *J.*, 1958, 2458.
[6] Badger and Kimber, *J.*, 1960, 2746.
[7] Badger and Kimber, *J.*, 1960, 266.

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investigations [8] have shown that benzene is readily dehydrogenated to biphenyl; and other hydrocarbons including *m*- and *p*-terphenyl and triphenylene have been identified.[9] As more efficient methods of separation and of identification of polycyclic compounds are now available, the pyrolysis of benzene has been re-examined.

The pyrolysis was carried out by passing the hydrocarbon vapour, with nitrogen, through a silica tube filled with porcelain chips at 700°. Methane and ethylene were detected in the exit gases. The liquid tar formed (in 78·2% yield) was collected and analysed by gas–liquid chromatography, chromatography on alumina, on acetylated cellulose, and on acetylated paper, and by spectroscopy. The following compounds were identified in this tar (% composition w/w in parentheses): benzene (75·91), biphenyl (20·84), fluorene (0·08), phenanthrene (0·10), anthracene (0·13), *p*-terphenyl (1·02), *m*-terphenyl (0·37), fluoranthene (0·06), *o*-terphenyl (? trace), triphenylene (0·67), chrysene (0·13), and 3,4-benzofluoranthene (0·05).

Biphenyl is thus the major product and indeed it may be conveniently prepared by this method. The only other substance formed in relatively large amounts were *p*-terphenyl, *m*-terphenyl and triphenylene, all of which must be formed by further phenylation (and cyclodehydrogenation) of biphenyl. A very small amount of a compound believed to be *o*-terphenyl was detected; but the quantity was insufficient for positive identification.[10] It seems likely that the *o*-terphenyl formed by further phenylation of biphenyl is rapidly converted into triphenylene.

The remaining hydrocarbons identified in the tar were present in very small amounts, totalling only 0·5% of the tar. Some fission of the benzene ring does occur, as shown by the identification of methane and ethylene in the exit gases, and plausible schemes for the formation of the compounds found can be suggested. Thus fluorene and phenanthrene could be formed from biphenyl by reaction with a one-carbon unit and a two-carbon unit respectively. Fluoranthene could be formed from biphenyl and a four-carbon unit (followed by cyclodehydrogenation); and 3,4-benzofluoranthene could be formed by phenylation of phenanthrene (followed by cyclodehydrogenation).

Experimental

Benzene.—Benzene was purified by shaking it with concentrated sulphuric acid, water, dilute sodium hydroxide, and water. After drying over sodium, the benzene was distilled. No impurity could be detected by gas–liquid chromatography.

Pyrolysis.—Benzene (100 g.) was vaporised at 10 g./hr. and passed with nitrogen (½ c.c./sec.) through a silica tube (36 in. × 1 in.) packed with porcelain chips (3/8—1/4 in.) which was maintained at 700° in an electrically heated furnace.[12] The resulting yellow tar (78·2 g.) was collected. The gaseous products decolorised bromine water and neutral and alkaline permanganate.

Analysis.—The tar was distilled to give the fractions (*a*) b. p. 80—100°/760 mm. (58·2 g.), (*b*) b. p. 100—140°/760 mm. (1·2 g.), and (*c*) a residue (18·8 g.). Fractions (*a*) and (*b*) were examined by gas–liquid chromatography over Apiezon L supported on Celite (40—80 mesh; 1 : 4 w/w) as stationary phase, and nitrogen as carrier gas. No products other than benzene could be detected. The residue (*c*) was chromatographed on alumina (4 g. at a time), and sixteen fractions were collected. The first was examined by gas–liquid chromatography, and the remainder by chromatography on columns of partially acetylated cellulose, and on partially acetylated paper.[13] The following compounds were identified in the fractions enumerated:

[8] *E.g.*, Berthelot, *Bull. Soc. chim. France*, 1866, **6**, 272; *Ann. Chim. Phys.*, 1866, **9**, 451; *Z. Chem.*, 1866, 707; Schultz, *Annalen*, 1874, **174**, 201; Smith and Lewcock, *J.*, 1912, **101**, 1453.

[9] Bachmann and Clarke, *J. Amer. Chem. Soc.*, 1927, **49**, 2089.

[10] Cf. Kaplan and Petrov, *Zhur. priklad. Khim.*, 1960, **33**, 1226; Andrianov, Kvitner, and Titova (*J. Chem. Ind. U.S.S.R.*, 1937, **4**, 161) also isolated a substance provisionally regarded as *o*-terphenyl but the physical constants now known preclude this identification.

[11] Copeland, Dean, and McNeil, *J.*, 1960, 1687.

[12] Badger, Buttery, Kimber, Lewis, Moritz, and Napier, *J.*, 1958, 2449.

[13] Spotswood, *J. Chromatog.*, 1959, **2**, 90; 1960, **3**, 101.

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(1) biphenyl; (2) fluorene, phenanthrene, anthracene, *p*-terphenyl; (3) *p*-terphenyl, *m*-terphenyl, fluoranthene; (4) fluoranthene, *o*-terphenyl (?), triphenylene, (5) triphenylene, chrysene; (6) chrysene; (7—8) chrysene, 3,4-benzofluoranthene; (9—16) not identified.

Identifications.—Samples of the exit gases were collected in a gas cell for infrared analysis. Methane was identified by its spectrum in the 7·3—8·5 μ region (max. at 7·36, 7·42, 7·66, 7·73, 7·79, 7·81, 7·85, 7·90, 7·94, 7·98, 8·05, 8·11, 8·17, and 8·22 μ), and ethylene by its spectrum in the 9·0—11·5 μ region (max. at 9·91, 10·01, 10·11, 10·21, 10·31, 10·40, 10·51, 10·75, 10·83, 10·92, 11·01, 11·07, 11·16, and 11·25 μ).[14]

Compounds identified were as follows; spectral maxima agreed with those of authentic specimens or with the literature.

Benzene, isolated from fractions (*a*) and (*b*) by gas–liquid chromatography. The b. p. and retention time were identical with those of an authentic specimen.

Biphenyl, isolated from fraction (1) by recrystallisation from ethanol; $\lambda_{max.}$ 248 mμ; m. p. and mixed m. p. 70° (cf. ref. 9).

Fluorene, identified in fraction (2) after chromatography on partially acetylated cellulose; $\lambda_{max.}$ 261, 290, and 301 mμ.

Phenanthrene, isolated from fraction (2) by chromatography on partially acetylated cellulose; $\lambda_{max.}$ 243, 251, 275, 281, and 294 mμ; fluorescence max. 348, 362, and 382 mμ.

Anthracene, identified in fraction (2) by chromatography on partially acetylated cellulose; $\lambda_{max.}$ 252, 308, 323, 339, 355, and 376 mμ; fluorescence max. 380, 403, 427, and 450 mμ (cf. ref. 15).

p-Terphenyl, identified in fractions (2) and (3) by chromatography on partially acetylated cellulose; $\lambda_{max.}$ 280 mμ; fluorescence max. 342 mμ; m. p. and mixed m. p. 213—214° (cf. ref. 9).

m-Terphenyl, isolated from fraction (3); m. p. 85—86° (lit.,[9] 87°); $\lambda_{max.}$ 250 mμ (cf. ref. 16); fluorescence band at 317 mμ.

Fluoranthene, identified in fractions (3) and (4); $\lambda_{max.}$ 237, 245, 253, 262, 271, 288, 309, 324, 343, and 359 mμ; fluorescence max. 446 and 465 mμ.

o-Terphenyl (?), isolated from fraction (3) by chromatography on partially acetylated cellulose; $\lambda_{max.}$ 233 mμ (cf. ref. 17).

Triphenylene, isolated from fractions (4) and (5); $\lambda_{max.}$ 250, 257, 274, 286, 316, 331, and 340 mμ; fluorescence max. 352, 360, and 368 mμ; m. p. and mixed m. p. 195—197° (lit.,[9] 199°).

Chrysene, isolated from fractions (5—8); $\lambda_{max.}$ 242, 259, 267, 283, 294, 306, 320, 344, 350, and 361 mμ; fluorescence max, 360, 381, 401, and 425 mμ.

3,4-Benzofluoranthene, isolated from fractions (7—8); $\lambda_{max.}$ 238, 256, 266, 276, 289, 293, 301, 320, 338, 350, and 369 mμ; fluorescence max. 443 and 462 mμ.

Ultraviolet Spectra.—These were examined in 95% ethanol by using a Optica CF_4 recording spectrophotometer.

Fluorescence Spectra.—These were examined in 95% ethanol in a Farrand recording spectrofluorometer.

We thank Dr. R. W. L. Kimber for many helpful discussions of this and the following paper. The work described in both papers has been carried out during the tenure of a grant from the Damon Runyon Memorial Fund, and we are also grateful to the Anti-Cancer Campaign Committee of the University of Adelaide for a maintenance grant (to J. N.).

UNIVERSITY OF ADELAIDE, AUSTRALIA. [*Received, February 20th*, 1961.]

[14] American Petroleum Institute Research Project 44, I.R. Spectral Data.
[15] Sawicki, Hauser, and Stanley, *Internat. J. Air Poll.*, 1960, **2**, 253.
[16] Friedel and Orchin, "Ultraviolet Spectra of Aromatic Compounds," Wiley, New York, 1951; Clar, "Aromatische Kohlenwasserstoffe," Springer, Berlin, 1952.
[17] Mueller and Pickens, *J. Amer. Chem. Soc.*, 1950, **72**, 3626.

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662. *The Formation of Aromatic Hydrocarbons at High Temperatures. Part XIII.* The Pyrolysis of 3-Vinylcyclohexene.*

By G. M. Badger and J. Novotny.

Pyrolysis of 3-vinylcyclohexene (a postulated intermediate in the formation of 3,4-benzopyrene at high temperatures) at 700° yields a tar in which 38 compounds have been identified. Mechanisms for the formation of some of these are discussed.

As a working hypothesis it was suggested that the carcinogenic hydrocarbon 3,4-benzopyrene may be formed at high temperatures by a step-wise synthesis from a two-carbon unit.[1] 3-Vinylcyclohexene is a possible intermediate,[2] and it therefore seemed of interest to examine its pyrolysis.

The pyrolysis was carried out by passing vinylcyclohexene vapour, with nitrogen, through a silica tube filled with porcelain chips at 700°. Much of the material was decomposed to gaseous products, among which only methane and ethylene have been identified. The semi-solid tar (obtained in 44·0% yield) was collected and analysed by gas–liquid chromatography, chromatography on alumina, acetylated cellulose, and acetylated paper, and by ultraviolet and fluorescence spectroscopy. The following compounds were identified (% by wt. in parentheses): Benzene (43·67); toluene (16·12); ethylbenzene (0·22); *p*-xylene (1·83); styrene (3·14); indene (0·48); naphthalene (13·16); 1- and 2-methylnaphthalene (3·67); biphenyl (3·44); 4,4′-dimethylbiphenyl (0·06); bibenzyl (0·31); stilbene (0·11); acenaphthylene (1·06); phenanthrene (1·84); fluorene (1·00); anthracene (0·64); pyrene (1·31); fluoranthene (0·34); 2,3-benzofluorene (0·70); 1,2-benzanthracene (0·34); 2,2′-binaphthyl (0·15); 1,2-benzofluorene (0·58); chrysene (0·42); triphenylene (0·11); perylene (0·13); 1,2-benzopyrene (0·31); 1,2:5,6-dibenzanthracene (0·13); 10,11-benzofluoranthene (0·22); 3,4-benzopyrene (0·48); 3,4-benzofluoranthene (0·27); 4,5-(*o*-phenylene)fluoranthene (indeno[1,2,3-*cd*]fluoranthene) (0·18); 11,12-benzofluoranthene (0·38); 1,12-benzoperylene (0·04); anthanthrene (0·15); 2,3-(*o*-phenylene)pyrene (indeno[1,2,3-*mn*]pyrene) (0·38); 3,4:9,10-dibenzopyrene (dibenzo[*a*,*i*]-pyrene) (0·05); and 3,4-benzotetraphene (0·08).

At the high temperature involved, abstraction of a hydrogen atom from a reactive allylic position in vinylcyclohexene must be an important initial process, giving the radicals (I) and (II). Moreover, carbon–carbon single bonds are known to have bond-dissociation energies of about 80 kcal./mole,[3] and such bonds should therefore undergo ready scission at 700° to give CH_2=CH· and the cyclohexenyl radical (III). Several other radicals might be formed by rupture of the ring and/or further scission. In this way the radicals (IV—XV) would all be expected as initial decomposition products of vinylcyclohexene.

These expected scission products show many similarities to the radicals which could be formed by the pyrolysis of buta-1,3-diene, and it is significant that the products obtained by pyrolysis of 3-vinylcyclohexene and buta-1,3-diene show a striking resemblance.[4] The formation of all the major products can be explained by suitable reactions of these radicals.

Benzene could be formed from (III) by dehydrogenation, and from (IX) or (XI) by cyclodehydrogenation. Cyclodehydrogenation of (XII), or reaction of (III) with methyl radicals (followed by dehydrogenation) could account for the large yield of toluene, and a similar mechanism could lead to bibenzyl and (by dehydrogenation) to stilbene and phenanthrene. A much more important route to phenanthrene could be by reaction of (I) and (III), followed by dehydrogenation. *p*-Xylene could be formed by the dimerisation

* Part XII, preceding paper.

[1] Badger, Buttery, Kimber, Lewis, Moritz, and Napier, *J.*, 1958, 2449.
[2] Badger, Kimber, and Spotswood, *Nature*, 1960, **187**, 663.
[3] Steacie, "Atomic and Free Radical Reactions," Reinhold, New York, 1954; Braude and Nachod, "Determination of Organic Structures by Physical Methods," Academic Press, New York, 1955.
[4] Badger and Spotswood, *J.*, 1960, 4431.

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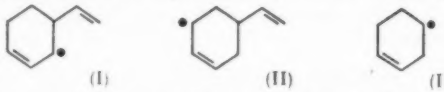
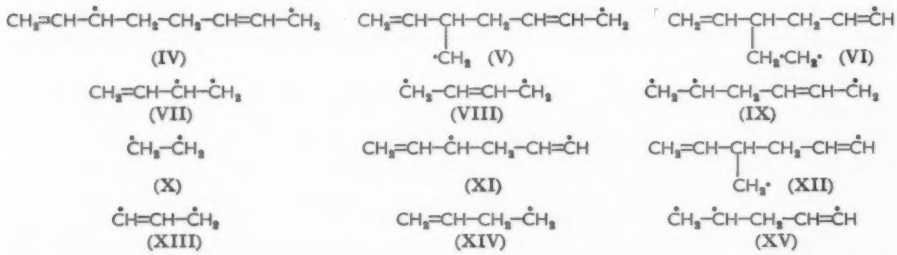
of two (XIV) radicals, followed by dehydrogenation. Dehydrogenation of vinylcyclohexene itself could account for the observed styrene; but the relatively small yield of this product shows that the scission of carbon–carbon bonds must be a much more important reaction at 700° than dehydrogenation.

The small amount of indene obtained could be formed by reaction of (III) with (XIII), followed by dehydrogenation; and naphthalene could be similarly formed from (III) and



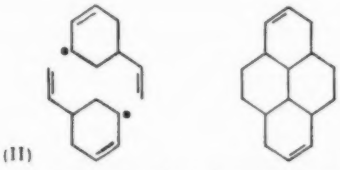
(I) (II) (III)



(IV) (V) (VI) (VII) (VIII) (IX) (X) (XI) (XII) (XIII) (XIV) (XV)

(VII), (VIII), or (XIV). Biphenyl could be obtained from two cyclohexenyl radicals (III), followed by dehydrogenation; and 4,4′-dimethylbiphenyl could be formed by dimerisation of two benzyl radicals. The relatively small yield of fluoranthene is somewhat surprising as it would be thought that this compound could arise by the dimerisation of two radicals of type (I).

The pyrolysis of naphthalene has been shown to yield the three isomeric binaphthyls, together with perylene, 10,11-benzofluoranthene, and 11,12-benzofluoranthene.[5] In the present work these products are almost certainly formed from naphthalene-type intermediates by similar dehydrogenations. In the same way the two *o*-phenylenepyrenes identified among the products must be formed by the cyclodehydrogenation of phenylpyrenes.[6]



(II) (XVI)

As expected, both 1,2-benzopyrene and 3,4-benzopyrene were found among the products (0·31 and 0·48% respectively), while pyrene was present to the extent of 1·31%. This agrees with the earlier conclusion [2] that tars embodying high yields of pyrene (for example, those formed by pyrolysis of acetylene, butadiene, or n-butylbenzene) also contain relatively large amounts of 3,4-benzopyrene. A tentative conclusion would be that dimerisation of two vinylcyclohexene radicals (II) would give a hydropyrene (XVI). This could suffer dehydrogenation to pyrene, or reaction with a four-carbon unit, followed by dehydrogenation, to give 3,4-benzopyrene.

Experimental

3-*Vinylcyclohexene*.—This was prepared by the thermal dimerisation of buta-1,3-diene as described by Ziegler and Wilms.[7] It had b. p. 131—132°, n_D^{14} 1·4672, n_D^{17} 1·4660 (lit.,[8] n_D^{20} 1·4653), and no impurities could be detected by gas–liquid chromatography.

[5] Lang, Buffleb, and Kalowy, *Chem. Ber.*, 1957, **90**, 2888, 2894; 1958, **91**, 2686; 1960, **93**, 303.
[6] Badger and Spotswood, *J.*, 1960, 4420.
[7] Ziegler and Wilms, *Annalen*, 1950, **567**, 28; 1954, **589**, 148.
[8] Reed, *J.*, 1951, 685.

Vol. 1960, page 3405, line 8, *for* [1-^{14}C]mannose *read* [^{14}C]mannose; page 3408, line 2, *for* D-[1-^{14}C]-mannose *read* D[^{14}C]-mannose; page 3409, Fig. 8, the scale for the rate of formation of carbon dioxide is 10^{10} molecules; page 3411, lines 3 and 6, *for* [^{14}C] *read* [1-^{14}C].

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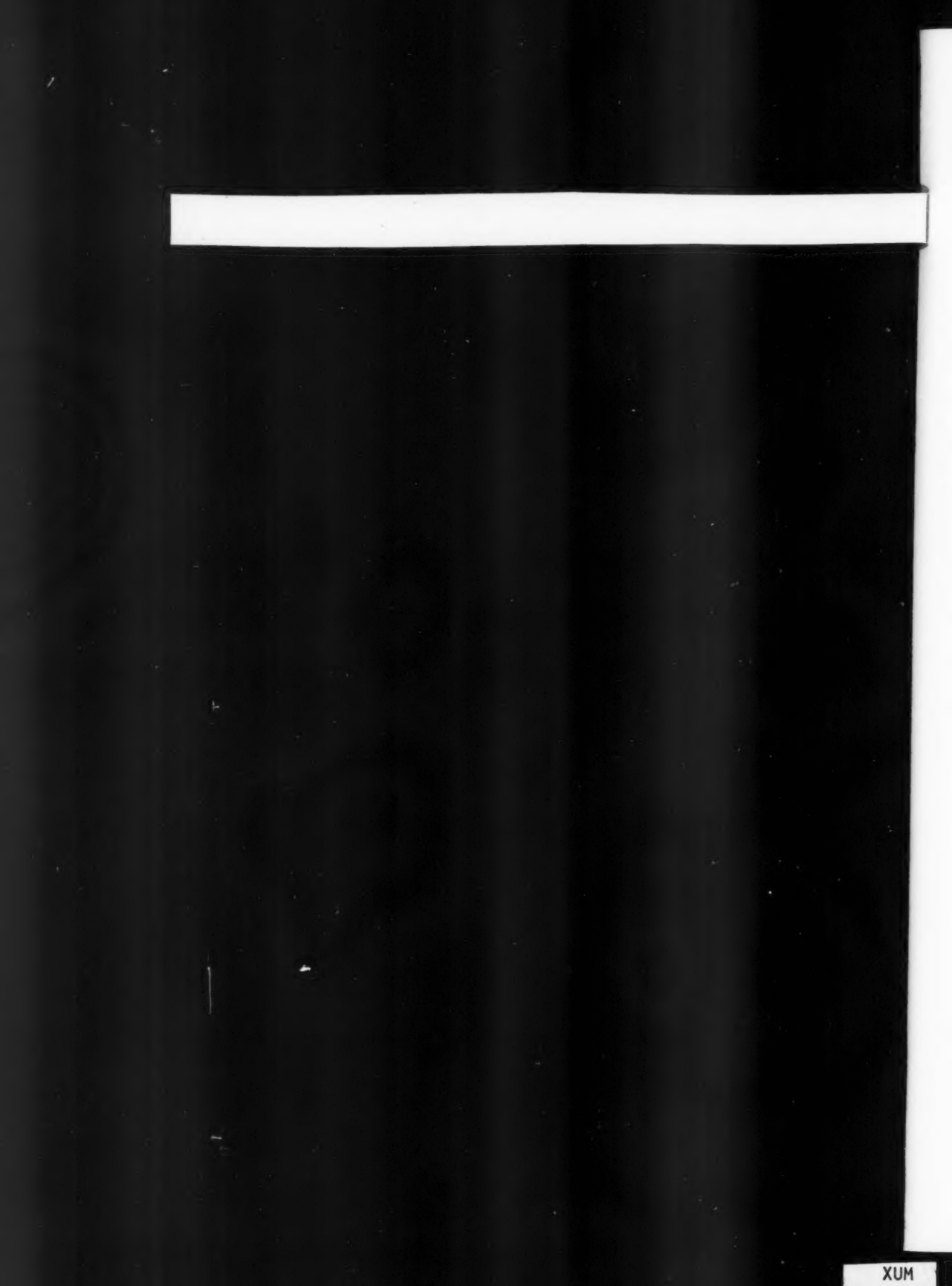

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Pyrolysis.—3-Vinylcyclohexene (50 g.) was vaporised at 7 g./hr. in a flash evaporator (maintained at 360°), and carried with a stream of nitrogen (1 c.c./sec.) through a silica tube (36 in. × 1 in.) packed with porcelain chips (3/8—1/4 in.) which was maintained at 700° in an electrically heated furnace.[1] The resulting dark brown fluid tar (22 g.), and samples of the exit gases, were collected.

Analysis.—The tar was distilled to give fractions (*a*) b. p. 80—100°/760 mm. (11·1 g.), (*b*) b. p. 100—140°/760 mm. (2·3 g.), (*c*) b. p. 40—90°/30 mm. (1·08 g.), (*d*) b. p. 90—130°/30 mm. (3·2 g.), and (*e*) a residue (4·4 g.). Fractions (*a*—*d*) were examined by gas–liquid chromatography (as in the preceding paper). Peaks corresponding to benzene, toluene, ethylbenzene, *p*-xylene, styrene, and indene, naphthalene, 1- and 2-methylnaphthalene, and biphenyl were observed. The residue (*e*) was chromatographed on a column of Spence alumina and seventeen fractions were collected. Fractions 1—3 were further examined by gas–liquid chromatography, and the remainder by chromatography on columns of partially acetylated cellulose and partially acetylated paper.[9] The following compounds were identified in the fractions enumerated: (1) naphthalene, 1- and 2-methylnaphthalene; (2) naphthalene, 1- and 2-methylnaphthalene, biphenyl, 4,4′-dimethylbiphenyl, bibenzyl; (3) biphenyl, stilbene; (4) acenaphthylene, phenanthrene; (5) acenaphthylene, phenanthrene, fluorene; (6) phenanthrene, anthracene, pyrene; (7) phenanthrene, pyrene, fluoranthene; (8) 2,3-benzofluorene, fluoranthene, 1,2-benzanthracene, 2,2′-binaphthyl; (9) 2,3-benzofluorene, 1,2-benzofluorene, 1,2-benzanthracene; (10) 2,3-benzofluorene, 1,2-benzofluorene, 1,2-benzanthracene, chrysene; (11) 2,3-benzofluorene, 1,2-benzofluorene, triphenylene, perylene, 1,2-benzopyrene, 1,2:5,6-dibenzanthracene, chrysene; (12) perylene, 1,2-benzopyrene, 1,2:5,6-dibenzanthracene, chrysene, 10,11-benzofluoranthene, 3,4-benzopyrene; (13) chrysene, 10,11-benzofluoranthene, 3,4-benzofluoranthene, 4,5-(*o*-phenylene)fluoranthene, 3,4-benzopyrene; (14) 11,12-benzofluoranthene, 10,11-benzofluoranthene, 3,4-benzofluoranthene, 4,5-(*o*-phenylene)fluoranthene, 3,4-benzopyrene; (15) 1,12-benzoperylene, anthanthrene, 2,3-(*o*-phenylene)pyrene, 3,4-benzopyrene; (16—17) 3,4:9,10-dibenzopyrene, anthanthrene, 3,4-benzotetraphene, 2,3-(*o*-phenylene)pyrene.

Identifications.—The gaseous products were collected and examined by infrared spectroscopy. Methane was identified by its spectrum in the 7·3—8·5 μ region (max. at 7·41, 7·48, 7·67, 7·78, 7·81, 7·86, 7·93, 8·04, 8·10, 8·16, and 8·21 μ), and ethylene by its spectrum in the 10·0—11·5 μ region (max. at 10·01, 10·11, 10·21, 10·30, 10·40, 10·50, 10·60, 10·73, 10·82, 10·90, 10·99, 11·06, 11·13, and 11·24 μ).[10]

The following were also identified; spectral data were in agreement with those of authentic specimens or with the literature.

Benzene, isolated from fractions (*a*) and (*b*) by gas–liquid chromatography; $\nu_{max.}$ (liquid film) 3·19, 3·80, 4·21, 4·41, 5·00, 5·41, 5·60, 5·89, 6·51, 6·76, 7·13, 8·50, and 9·16 μ.

Toluene, isolated from fractions (*a*) and (*b*); $\nu_{max.}$ (liquid film) 3·29, 3·42, 3·48, 3·64, 5·14, 5·38, 5·55, 5·76, 6·24, 6·56, 6·69, 6·84, 7·26, 9·25, 9·70, 13·73, and 14·42 μ.

Ethylbenzene, identified in fractions (*b*) and (*c*) by comparison of retention time ratio with that of an authentic specimen.

p-Xylene, isolated from fractions (*b*) and (*c*) by gas–liquid chromatography; $\nu_{max.}$ (liquid film) 3·30, 3·42, 3·48, 3·65, 5·45, 5·58, 6·14, 6·58, 6·87 7·25, 8·20, 8·92, 9·06, 9·58, 9·78, 10·04, and 12·59 μ.

Styrene, isolated from fractions (*b*) and (*c*) by gas–liquid chromatography; $\nu_{max.}$ (liquid film) 3·20, 5·10, 5·30, 5·50, 5·70, 5·90, 6·11, 6·22, 6·32, 6·70, 6·90, 7·08, 7·50, 7·60, 7·73, 8·32, 9·26, 9·78, 10·10, 11·00, 11·90, 12·90, and 14·40 μ.

Indene, identified in fraction (*c*) by gas–liquid chromatography by comparison of retention time ratio with that of an authentic specimen.

Naphthalene, isolated from fractions (*d*), 1, and 2 by gas–liquid chromatography; $\lambda_{max.}$ 248, 257, 266, 275, 285, and 311 mμ, m. p. and mixed m. p. 78—80°; fluorescence max. 330 mμ.

1- and 2-Methylnaphthalene, identified in fractions (*d*), 1, and 2, by gas–liquid chromatography by comparison of their retention time ratios with those of authentic specimens; attempts to separate the isomers were unsuccessful, but the predominance of the 2-isomer may be inferred from the shape of the curve.

Biphenyl, isolated from fractions (*d*), 1, 2, and 3 by gas–liquid chromatography; m. p. and mixed m. p. 69—70°; $\lambda_{max.}$ 250 mμ.

[9] Spotswood, *J. Chromatog.*, 1959, **2**, 90; 1960, **3**, 101.
[10] American Petroleum Institute Research Project 44, I.R. Spectral Data.

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4,4′-Dimethylbiphenyl, identified in fraction 2 by gas–liquid chromatography and comparison of its retention time ratio with that of an authentic specimen.

Bibenzyl, identified in fraction 2 on gas–liquid chromatography and comparison of its retention time ratio with that of an authentic specimen.

Stilbene, isolated from fraction 3 by gas–liquid chromatography; m. p. and mixed m. p. 120—122°.

Acenaphthylene, isolated from fractions 4 and 5 by chromatography on partially acetylated cellulose; $\lambda_{max.}$ 229, 258, 266, 276, 309, 323, 334, and 340 mμ.

Phenanthrene, isolated from fractions 4—7 by chromatography on partially acetylated cellulose; m. p. and mixed m. p. 96—98°; $\lambda_{max.}$ 243, 252, 275, 282, 294, 310, 317, 324, 331, 339, and 346 mμ; fluorescence max, 350, 363, and 383 mμ.

Fluorene, isolated from fraction 5 by chromatography on partially acetylated cellulose; $\lambda_{max.}$ 260, 290, and 301 mμ; fluorescence max. 320 mμ.

Anthracene, isolated from fraction 6 by chromatography on partially acetylated cellulose; $\lambda_{max.}$ 246, 253, 308, 323, 339, 357, and 377 mμ; fluorescence max. 380, 403, 430, and 460 mμ.

Pyrene, isolated from fractions 6 and 7 by chromatography of partially acetylated cellulose; $\lambda_{max.}$ 231, 241, 253, 263, 274, 306, 319, 335, 351, 358, 364, and 373 mμ; fluorescence max. 385 and 395 mμ; m. p. and mixed m. p. 146—147°.

Fluoranthene, isolated from fractions 7 and 8 by chromatography on partially acetylated cellulose; m. p. and mixed m. p. 105—107°; $\lambda_{max.}$ 236, 253, 263, 273, 278, 282, 288, 309, 323, 342, and 360 mμ; fluorescence max. 446 and 466 mμ.

2,3-Benzofluorene, identified in fractions 8—11 by chromatography on partially acetylated cellulose, followed by chromatography on partially acetylated paper; $\lambda_{max.}$ 255, 264, 273, 285, 304, 317, 325, 333, and 340 mμ; fluorescence max. 342 and 358 mμ.

1,2-Benzanthracene, isolated from fractions 8—10 by chromatography on partially acetylated cellulose; $\lambda_{max.}$ 222, 227, 256, 268, 278, 289, 300, 315, 326, 341, 358, 365, 374, and 384 mμ; fluorescence max. 377, 396, 418, and 445 mμ.

2,2′-Binaphthyl, isolated from fraction 8 by chromatography on partially acetylated cellulose, followed by chromatography on acetylated paper; $\lambda_{max.}$ 255 and 309 mμ; fluorescence max. 352 and 365 mμ.

1,2-Benzofluorene, isolated from fractions 9—11 by chromatography on a column of acetylated cellulose and then on acetylated paper; $\lambda_{max.}$ 254, 263, 294, 304, 317, 330, and 343 mμ; fluorescence max, 342 and 350 mμ (cf. ref. 11).

Chrysene, isolated from fractions 10—13 by chromatography on acetylated cellulose; $\lambda_{max.}$ 242, 259, 267, 283, 294, 306, 320, 344, 351, and 363 mμ; fluorescence max. 359, 374, 395, and 419 mμ; m. p. and mixed m. p. 253—255°.

Triphenylene, isolated from fraction 11 by chromatography on partially acetylated cellulose; $\lambda_{max.}$ 250, 257, 275, 286, 316, 330, and 341 mμ; fluorescence max. 352, 361, and 369 mμ.

Perylene, isolated from fractions 11 and 12 by chromatography on acetylated cellulose followed by chromatography on acetylated paper; $\lambda_{max.}$ 245, 253, 263, 367, 386, 407, and 435 mμ; fluorescence max. 436, 460, and 493 mμ.

1,2-Benzopyrene, isolated from fractions 11 and 12 by chromatography on acetylated cellulose followed by chromatography on acetylated paper; $\lambda_{max.}$ 238, 258, 268, 278, 289, 305, 317, 333, and 366 mμ in substantial agreement with the literature;[12] fluorescence max. 385 and 405 mμ (cf. ref. 11).

1,2:5,6-Dibenzanthracene, isolated from fractions 11 and 12 by chromatography on acetylated cellulose; $\lambda_{max.}$ 231, 288, 298, 319, 335, 348, 374, and 383 mμ; fluorescence max. 377, 388, and 400 mμ.

10,11-Benzofluoranthene, isolated from fractions 12—14 by chromatography on acetylated cellulose; $\lambda_{max.}$ 241, 282, 293, 309, 318, 333, 345, 365, 376, and 383 mμ; peaks at 258 and 267 mμ, probably due to chrysene, were also observed. The fluorescence spectrum showed maxima at 480 and 508 mμ.

3,4-Benzopyrene, isolated from fractions 12—15 by chromatography on partially acetylated cellulose; $\lambda_{max.}$ 255, 266, 273, 284, 297, 332, 347, 365, 379, 385, and 404 mμ; fluorescence max. 397, 422, 448, and 478 mμ.

[11] Sawicki, Hauser, and Stanley, *Internat. J. Air Poll.*, 1960, **2**, 253.

[12] Clar, "Aromatische Kohlenwasserstoffe," 2nd edn., Springer, Berlin, 1952; Friedel and Orchin, "Ultraviolet Spectra of Aromatic Compounds," Wiley, New York, 1951.

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3,4-Benzofluoranthene, isolated from fraction, 14 by chromatography on acetylated cellulose, had m. p. and mixed m. p. 160—164°; $\lambda_{max.}$ 239, 256, 266, 276, 290, 294, 301, 320, 339, 351, and 369 mμ; fluorescence max. 398, 426, and 445 mμ.

4,5-(*o*-Phenylene)fluoranthene, identified in fractions 13 and 14 by chromatography on acetylated cellulose followed by chromatography on acetylated paper; $\lambda_{max.}$ 253, 262, 272, 368, 380, 387, 402, and 411 mμ (cf. ref. 6).

11,12-Benzofluoranthene, identified in fraction 14 after chromatography on acetylated cellulose; $\lambda_{max.}$ 238, 247, 269, 283, 297, 309, 361, 380, and 402 mμ; fluorescence max. 400, 427, and 455 mμ (cf. ref. 6).

1,12-Benzoperylene, isolated from fraction 15 by chromatography on acetylated cellulose; $\lambda_{max.}$ 268, 276, 289, 300, 315, 325, 330, 345, 363, and 383 mμ; fluorescence max. 390, 402, 414, 426, and 436 mμ.

Anthanthrene, isolated from fractions 15—17 by chromatography on acetylated cellulose followed by chromatography on acetylated paper; $\lambda_{max.}$ 233, 256, 259, 295, 308, 365, 382, 402, 407, 422, and 431 mμ; fluorescence max. 428, 454, and 484 mμ.

2,3-(*o*-Phenylene)pyrene, isolated from fractions 15—17 by chromatography on acetylated cellulose followed by chromatography on acetylated paper; $\lambda_{max.}$ 251, 269, 277, 292, 304, 315, 360, 376, 385, 402, 408, 422, and 431 mμ (cf. refs. 5, 6); fluorescence max. 476 and 504 mμ.

3,4:9,10-Dibenzopyrene, isolated from fractions 16—17 by chromatography on acetylated cellulose followed by chromatography on acetylated paper; $\lambda_{max.}$ 234, 242, 273, 283, 296, 315, 331, 353, 373, and 393 mμ; fluorescence max. 428, 456, 489, and 520 mμ.

3,4-Benzotetraphene, isolated from fractions 16—17 by chromatography on acetylated cellulose followed by chromatography on acetylated paper; $\lambda_{max.}$ 248, 277, 287, 304, 318, 332, 345, 363, 382, and 390 mμ; fluorescence max. 392, 414, and 440 mμ.

Spectra.—See preceding paper.

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663. *The Formation of Aromatic Hydrocarbons at High Temperatures. Part XIV.* The Pyrolysis of* [α-^{14}C]*Ethylbenzene.*

By G. M. BADGER and R. W. L. KIMBER.

Pyrolysis of [α-^{14}C]ethylbenzene at 700° has given a tar from which several compounds have been isolated and submitted to radiochemical assay. The results indicate that very little randomisation occurs, that the benzene ring system is very stable, that phenanthrene is probably formed by interaction of a C_6–C_2 unit and a C_6 unit (and not from two C_6–C_1 units), that anthracene is probably formed by rearrangement from phenanthrene, that 3,4-benzofluoranthene is formed by phenylation of phenanthrene followed by cyclodehydrogenation, and that at least two mechanisms must be involved in the formation of toluene and of pyrene.

PREVIOUS investigations in this series have shown that polycyclic aromatic hydrocarbons (including the carcinogenic 3,4-benzopyrene) are formed by the pyrolysis of simpler hydrocarbons.[1-8] The compounds pyrolysed have included acetylene,[4] butadiene,[6] ethylbenzene,[5]

* Parts XII and XIII, preceding papers.

[1] Badger, Buttery, Kimber, Lewis, Moritz, and Napier, *J.*, 1958, 2449; Badger and Kimber, *J.*, 1958, 2453; Badger and Kimber, *J.*, 1958, 2455; Badger and Buttery, *J.*, 1958, 2458; Spotswood, *J.*, 1960, 4427; Badger, Kimber, and Spotswood, *Nature*, 1960, **187**, 663.
[2] Badger and Spotswood, *J.*, 1959, 1635; Badger and Kimber, *J.*, 1960, 2746.
[3] Badger and Kimber, *J.*, 1960, 266.
[4] Badger, Lewis, and Napier, *J.*, 1960, 2825.
[5] Badger and Spotswood, *J.*, 1960, 4420.
[6] Badger and Spotswood, *J.*, 1960, 4431.
[7] Badger and Novotny, *J.*, part XII.
[8] Badger and Novotny, *J.*, part XIII.

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n-butylbenzene,[5] and tetralin;[3] and mechanisms for the formation of the polycyclic compounds have been advanced. Some theoretically possible mechanisms have been excluded as major routes to some compounds by consideration of the relative yields; but in other cases two or more mechanisms have seemed equally probable. To obtain more precise information we have investigated the use of ^{14}C-labelled compounds. At the high temperatures involved in pyrolyses it seemed that sufficient randomisation of the active carbon atoms might occur to make this approach useless, and as a preliminary test of the method the pyrolysis of [α-^{14}C]ethylbenzene, $Ph\cdot{}^{14}CH_2\cdot CH_3$, was undertaken.

[*carbonyl*-^{14}C]Acetophenone was prepared by a Friedel–Crafts reaction from benzene and sodium [*carboxy*-^{14}C]acetate, and reduced to [α-^{14}C]ethylbenzene by catalytic hydrogenation. This labelled ethylbenzene was then pyrolysed under conditions similar to those used for the inactive compound.[5] Several compounds were isolated from the resulting tar and submitted to radiochemical assay, the activities being expressed as relative molar activities[9] (which are linearly proportional to the number of labelled carbon atoms per molecule). The following compounds were isolated and analysed in this way (the number of labelled carbon atoms is given in parentheses): benzene (0·024), toluene (0·74), styrene (1·07), naphthalene (2·00), biphenyl (0·045), phenanthrene (1·05), anthracene (1·03), pyrene (2·4, 2·65), chrysene (3·14), and 3,4-benzofluoranthene (0·91). Other compounds known to be formed in this pyrolysis[5] could not be isolated in sufficient amount or in suitable purity for radiochemical analysis.

It has been generally considered on theoretical grounds, and on practical evidence,[7,10] that benzene is relatively stable even at 700°, and that the ring system does not break to a significant extent. However, the possibility of ring fission followed by re-formation had not been entirely eliminated. Groll[11] suggested that the initial step in pyrolyses involves breakdown to acetylene which then reacts with itself to form other compounds. Weizmann *et al.*[12] regarded butadiene as the precursor of the polycyclic compounds. It is therefore significant that the benzene isolated in the present work was found to be practically inactive; breakdown and resynthesis of the benzene ring must therefore occur only to a very small extent at 700°. This conclusion is supported by the inactivity of the biphenyl isolated, for this product must be formed by a termination reaction between two phenyl radicals, or by a propagation reaction brought about by phenyl-radical attack on ethylbenzene, with elimination of an ethyl radical.

Dehydrogenation of ethylbenzene by thermal fission of two C–H bonds would give styrene, and this is supported by the fact that the isolated styrene had one active carbon atom.

However, as previously discussed,[5] the scission of a C–C bond is a process of lower energy than C–H scission, and ethylbenzene must therefore be expected to break down very readily according to schemes (1) and (2a) to give benzyl, methyl, phenyl, and ethyl radicals. Scission to give a two-carbon unit (*i.e.*, scheme 2a) seems to be preferred in pyrolyses, since ethyl- and butyl-benzene both give larger yields of benzene than toluene, while pyrolysis of propylbenzene gives a larger yield of toluene.[5] On the other hand, the ethyl radicals could either react as such or undergo further scission (equation 2b) to methyl radicals. Evidence on this point has been provided by an examination of the exit gases: hydrogen, methane, and ethylene (plus ethane) are present in the approximate ratio 4 : 3 : 1. This low proportion of ethylene (plus ethane) suggests that ethyl radicals react more readily than methyl radicals, or that they undergo this further scission to methyl radicals and finally form the more stable compound, methane. The large proportion of hydrogen is expected in view of the predominance of dehydrogenation and cyclodehydrogenation at high temperatures. It must be concluded, therefore, that both

[9] Birch, Massy-Westropp, Rickards, and Smith, *J.*, 1958, 360.
[10] Egloff, "Reactions of Pure Hydrocarbons," Reinhold Publ. Corp., New York, 1937, p. 498.
[11] Groll, *Ind. Eng. Chem.*, 1933, **25**, 784.
[12] Weizmann *et al.*, *Ind. Eng. Chem.*, 1951, **43**, 2312, 2318, 2322, 2325.

labelled and unlabelled methyl radicals are formed in the pyrolysis, and that the latter predominate.

$$Ph\cdot{}^{*}CH_2\cdot CH_3 \longrightarrow Ph\cdot{}^{*}CH_2\cdot + \cdot CH_3 \quad \ldots\ldots\ldots\ldots (1)$$

$$Ph\cdot{}^{*}CH_2\cdot CH_3 \xrightarrow{a} Ph\cdot + \cdot{}^{*}CH_2\cdot CH_3 \xrightarrow{b} \cdot{}^{*}CH_3 + \cdot CH_3 \quad \ldots\ldots (2)$$

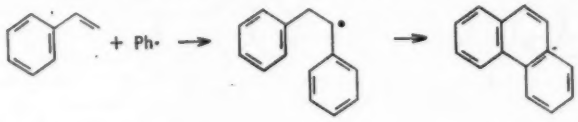
Now if toluene is formed by scission according to scheme (1) and hydrogenation of the benzyl radical, then it should have activity corresponding to one labelled atom. If it is formed by reaction of a methyl radical with a phenyl radical (or benzene) it should have activity corresponding to less than 0·5 labelled atom. Experimentally it was found that the activity corresponded to 0·74 labelled atom, and it seems that both mechanisms operate, the first predominating.

Chain re-synthesis has been postulated [5] to account for the formation of naphthalene from ethylbenzene. Reaction of a phenethyl radical with ethylene, for example, would be expected to give a phenylbutyl radical (scheme 3) and hence naphthalene; and several variants of this process could also occur. This mechanism would require the resulting naphthalene to have two labelled atoms, and this was found to be the case.

$$Ph\cdot{}^{*}CH_2\cdot CH_2\cdot + {}^{*}CH_2{=}CH_2 \longrightarrow Ph\cdot{}^{*}CH_2\cdot CH_2\cdot{}^{*}CH_2\cdot CH_2\cdot \quad \ldots\ldots (3)$$

For formation of phenanthrene one possible route would involve a chain termination between two benzyl radicals, and cyclodehydrogenation of the resulting bibenzyl; or the bibenzyl could be formed by chain propagation from toluene and a benzyl radical. This route was earlier considered [5] to be unimportant in view of the small yield of phenanthrene furnished by pyrolysis of toluene, a conclusion which has been confirmed by the present work. This route should yield phenanthrene with radioactivity corresponding to two labelled carbon atoms; but the phenanthrene obtained contained only one labelled atom. Another possible route, involving reaction between naphthalene and a four-carbon unit (such as a butadienyl radical), must also be excluded as this would yield phenanthrene having approximately four labelled atoms.

The most probable route involves the action of a phenyl radical on a C_6–C_2 unit (such as ethylbenzene, styrene, a phenethyl radical or a styryl radical) and cyclodehydration of the product (scheme 4). Such a scheme would give phenanthrene having one labelled atom in agreement with experiment. It may be noted, however, that the present results



····· (4)

do not preclude the possibility that some phenanthrene may be formed from biphenyl and a two-carbon unit; but consideration of the relative yields of biphenyl and phenanthrene formed by pyrolyses of toluene, ethylbenzene, n-propylbenzene, and n-butylbenzene [5] indicates that this route cannot be important.

It is also noteworthy that oxidative degradation of the phenanthrene isolated, followed by decarboxylation of the resulting biphenic acid, gave biphenyl having practically no radioactivity. Randomisation must therefore have been practically non-existent.

Anthracene could conceivably be formed from two benzyl radicals, or from naphthalene (or its equivalent) and a four-carbon unit. The former route should give a product having two labelled atoms, and the second a product having approximately four active atoms. As the anthracene isolated had activity corresponding to only one labelled atom neither of these routes can be important, and it seems likely that in this pyrolysis the anthracene is formed by thermal rearrangement of phenanthrene.[13]

[13] Orlow, *Ber.*, 1927, **60**, 1950.

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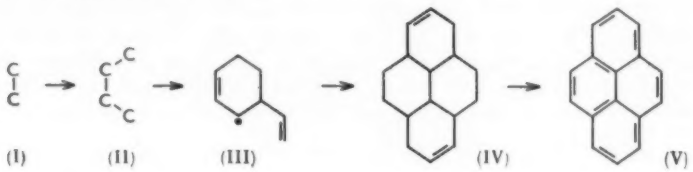
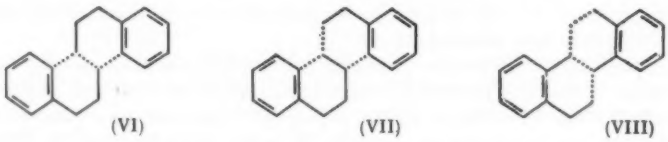
The mode of formation of pyrene cannot be determined with certainty by the present work. Various suggestions have been published: possible routes involve dimerisation of styrene (Badger and Buttery [1]), 3-vinylcyclohexenyl radicals,[6,8] or *m*-xylene,[14] or step-wise synthesis from a two-carbon unit.[11] The number of labelled carbon atoms found (approx. 2·5) suggests that more than one route may be important. A mechanism involving styrene as an intermediate would give pyrene having two labelled atoms; and one involving *m*-xylene would give pyrene having approximately three labelled atoms (as the *m*-xylene would presumably be formed by attack of methyl radicals on toluene)—the latter route seems very unlikely, for, although the pyrolysis of *m*-xylene is known to give pyrene,[14] *m*-xylene itself has not been identified among the products of the pyrolysis of ethylbenzene or of the other alkylbenzenes studied.[5]



(I) (II) (III) (IV) (V)

An alternative route to pyrene, involving step-wise synthesis from a two-carbon unit (I ⟶ V), should give pyrene having eight labelled atoms. The observed activity could then be explained if it is assumed that most is formed from styrene (or its equivalent) and the remainder by the route (I ⟶ V).

As previously postulated,[2,3] chrysene could be formed from two C_6–C_3 units (as VI), from a C_6–C_4 and a C_6–C_2 unit (as VII), and from two C_1–C_6–C_2 units (as VIII). Each



(VI) (VII) (VIII)

(IX) (X)

of these would give chrysene having three labelled atoms, in agreement with experiment, providing that chain-lengthening occurs by attack of a methyl radical on a C_6–C_2 unit (to give the C_6–C_3 or the C_1–C_6–C_2 unit), and not by attack of an ethyl radical on a C_6–C_1 unit. With these qualifications the original proposals still appear plausible.

3,4-Benzofluoranthene could conceivably be formed either by interaction of two C_6–C_4 units (as IX), or by cyclodehydrogenation of 9(or 1)-phenylphenanthrene (as X). In pyrolysis of [α-^{14}C]ethylbenzene the former route should yield 3,4-benzofluoranthene having four labelled atoms (as each C_6–C_4 unit would have two labelled atoms). The second route should also give 3,4-benzofluoranthene containing four active atoms if the phenylphenanthrene is formed from two C_6–C_4 units; but if the intermediate is formed by phenylation of phenanthrene then only one labelled atom would be expected. In fact the product showed activity corresponding to one radioactive carbon atom and the latter route therefore seems to be confirmed.

[14] Baker, McOmie, and Norman, *Chem. and Ind.*, 1950, 77.

Experimental

Radioactive Assay.—Specimens were assayed for radioactivity, with an end-window counter, as infinitely thick, solid samples of 1 cm.^{2} cross-sectional area;[15] and counting rates were corrected for background and dead time of the instrument. The counting equipment consisted of an EKCO automatic scaler type N530D, in conjunction with an EKCO probe unit type N558 and an EW3H Geiger tube. The counts per min. were determined by recording five readings each of 5 min. duration for each sample. All assays were usually repeated twice, either with a new sample or with the original sample repacked. In this way errors due to differences in packing, and to losses during dilution, were almost eliminated. The statistical counting error was calculated as standard deviations for each series of counts and was in no case greater than 1·5% (except for the practically inactive products). Van Slyke–Folch oxidations were carried out essentially as described in the literature;[16] however, the apparatus was adapted for oxidation of liquids by using sealed capillaries containing the material to be oxidised. The Van Slyke fluid was contained in a 2-neck 25 ml. flask. The second neck contained the capillary tube which, after evacuation of the system, was fractured on a lip protruding through the joint from the main part of the system, by twisting the flask.

The samples were prepared by the " pellet " technique.[15] It was found that the technique of gently rotating the press before removing it to prevent the pellet getting stuck was often unsatisfactory for some low-melting substances (*e.g.*, styrene dibromide, biphenyl, naphthalene). Quite clean separations were obtained, however, if the planchette was first cooled on a block of solid carbon dioxide for 4—5 sec., and the press warmed by immersion for a similar time in hot water and then dried. Difficulty due to static electrical effects for substances such as anthraquinone, chrysene, and 3,4-benzofluoranthene was overcome by grinding the material with a drop of water in an agate mortar. After pelleting, the sample was dried under an infrared lamp.

[carbonyl-^{14}C]*Acetophenone.*—Sodium [*carboxy*-^{14}C]acetate (1·0 mc; 20·4 mg.) was scraped from the phial with a spatula into a 3-neck flask. The phial was rinsed with ten 1 ml. portions of benzene, and the washings were poured into the reaction vessel (~98% transfer). Pure inactive anhydrous sodium acetate was added to give total acetate (2·46 g., 0·03 mole). Aluminium chloride (16·5 g., 0·12 mole) and benzene (5 ml.) were added, and the mixture stirred and refluxed for 8 hr., then worked up as in method I for the preparation of [*carbonyl*-^{14}C]-acetophenone described by Murray and Williams.[17] Final purification was effected by distillation in a vacuum line, to give [*carbonyl*-^{14}C]acetophenone (2·62 g., 85%), n_D^{15} 1·5353 (lit.,[18] n_D^{15} 1·5363)

[α-^{14}C]*Ethylbenzene.*—[*carbonyl*-^{14}C]Acetophenone (2·17 g.), "AnalaR " acetic acid (6 ml.), 70% perchloric acid (5 drops), and 5% palladium–charcoal (2 g.) were hydrogenated for 72 hr. at 50 lb./in.^{2} in a Cook and Son's low-pressure hydrogenator adapted for semimicro-work. The reaction mixture was filtered through a sintered-glass funnel, and the catalyst washed with ethanol (5 ml.). The filtrate was neutralised with sodium hydroxide solution and extracted with ether (2 × 10 ml.); the extract was washed with water, dried, and evaporated, and the residue diluted to 100 ml. with inactive ethylbenzene and then distilled, giving [α-^{14}C]ethylbenzene, b. p. 133—134°, n_D^{14} 1·4983 (lit.,[19] $n_D^{14\cdot5}$ 1·4983). Van Slyke–Folch oxidation gave barium carbonate which was collected for radioactive assay (Found: relative molar activity × 10^{-2}, 20·8 ± 0·19).

Degradation of [α-^{14}C]*Ethylbenzene.*—[α-^{14}C]Ethylbenzene (0·05 ml.) was diluted to 0·5 ml. with inactive material and degraded by side-chain bromination, followed by hydrolysis and permanganate oxidation to benzoic acid.[20] Recrystallisation from water gave [*carboxy*-^{14}C]-benzoic acid, m. p. 120·5—122° (Found: relative molar activity × 10^{-2}, 21·8 ± 0·70; 1*C requires 20·8).

Pyrolysis of [α-^{14}C]*Ethylbenzene.*—[α-^{14}C]Ethylbenzene (40 g.) was pyrolysed under similar

[15] Popjak, *Biochem. J.*, 1950, **46**, 560.
[16] Calvin, Heildelberger, Reid, Talbert, and Yankwich, " Isotopic Carbon," Wiley, New York, 1949, p. 92.
[17] Murray and Williams, " Organic Synthesis with Isotopes," Part I, Interscience Publ. Inc., New York, p. 662.
[18] Timmermans and Hennaut-Roland, *J. Chim. phys.*, 1935, **32**, 525.
[19] " Handbook of Physics and Chemistry," Chemical Rubber Publ. Co., Cleveland, Ohio, 1958, 834.
[20] Roberts, Ropp, and Neville, *J. Amer. Chem. Soc.*, 1955, **77**, 1764.

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conditions to those described for the inactive compound.[5] It was vaporised (8 drops/min.) and passed with nitrogen (1 ml./sec.) through the pyrolysis tube maintained at 700°. The resulting tar (19·5 g.) together with the chloroform washings from the pyrolysis tube was distilled, to give fractions (*a*) b. p. 80—140° (12·0 g.), (*b*) b. p. 80—120°/20 mm. (2·5 g.), and (*c*) a residue (4·25 g.).

Analysis.—Gas–liquid chromatography, chromatography on activated alumina and on columns of partially acetylated cellulose, and recrystallisation were used to separate and purify the compounds which were identified by m. p.s and ultraviolet and fluorescence spectra. Radioactive assay could only be carried out on compounds obtained pure in quantity such that dilution did not appreciably affect the accuracy of the determinations (usually not less than 5—10 mg. were required).

Exit Gases.—The infrared spectrum of a sample of the exit gases showed the presence of methane and ethylene. Further samples were analysed by gas–liquid chromatography in a Perkin–Elmer vapour fractometer. Comparison of retention times with those of standard samples of methane and ethylene gave the following analysis: methane ~18·3%, ethylene 4·8 ± 0·4%, ethane (?) 2 ± 0·4%, nitrogen ~50%, and (by difference) hydrogen ~24·9%. Hydrogen was used as the carrier gas. Therefore the gases formed in the pyrolysis were methane 36·6%, ethane (?) 4%, ethylene 9·6%, and hydrogen 49·8%. The ethane was provisionally identified by comparison with recorded retention times.

Fractions (a) and (b).—Fraction (*a*) was shown by gas–liquid chromatography in a Griffin and George vapour-phase chromatographic apparatus (mark II) to contain benzene, toluene, and styrene. Fraction (*b*) was found to contain mainly naphthalene and biphenyl. These compounds were separated and purified as described below.

Examination of Residue.—The residue (*c*) was chromatographed in a minimum amount of benzene–hexane (1 : 2) on alumina (Spence). Elution gave the following fractions (200 ml. each): with hexane, fractions 1—19; with benzene–hexane (1 : 10), fractions 20—47; with benzene–hexane (1 : 4), fractions 48—56; with benzene–hexane (1 : 2), fractions 57—63; with benzene–hexane (1 : 1), fractions 64—71, and with benzene–hexane (2 : 1), fractions 72—76. On the basis of their fluorescence and ultraviolet spectra, these fractions were recombined to give twelve main fractions. By the techniques described below for the individual compounds the following pure substances (or their derivatives) were isolated from seven of these fractions: fractions 1—10, naphthalene and biphenyl; fractions 11—22, phenanthrene; fractions 23—26, anthracene and pyrene; fractions 27—30, pyrene; fractions 51—55, chrysene; fractions 56—65 and 66—69, 3,4-benzofluoranthene.

Isolations.—Benzene. Fraction (*a*) was fractionated through a 10 cm. Vigreux column. Gas–liquid chromatography showed that the distillate contained 4—6% of toluene. Refractionation (twice) gave benzene, $n_D^{16\cdot5}$ 1·5033 (lit.,[21] n_D^{16} 1·5038). A sample (12 mg.) was oxidised by the Van Slyke–Folch technique and the resulting barium carbonate collected for radioactive assay (Found: relative molar activity × 10^{-2}, 0·5 ± 0·08).

Toluene. A portion of the combined residues from the fractionation of fraction (*a*) was chromatographed in the gas–liquid chromatograph, and the toluene fraction collected.[22] Further gas–liquid chromatography of a sample of this toluene showed it contained <2% of impurities. Van Slyke–Folch oxidation gave barium carbonate which was washed and collected for radioactive assay (Found: relative molar activity × 10^{-2}, 15·5 ± 0·14; 1*C requires 20·8).

Styrene. The combined residues from fraction (*a*), after the toluene had been removed, was shown by gas–liquid chromatography to contain approx. 20% of styrene. The portion not used for the toluene analysis was treated dropwise with bromine until a red colour persisted. On cooling, the dibromide separated. Recrystallisation from 80% ethanol (with charcoal) gave styrene dibromide (6 mg.), m. p. 66—68°. Dilution with inactive dibromide (24 mg.) gave sufficient material for radiochemical assay (Found: relative molar activity × 10^{-2}, 22·4 ± 0·26; 1*C requires 20·8).

Naphthalene. Fraction (*b*) was redistilled slowly on a water-bath under water-pump vacuum. Recrystallisation of the solid distillate gave naphthalene, m. p. 79—80° (Found: relative molar activity × 10^{-2}, 41·5 ± 0·01; 2*C requires 41·6).

Biphenyl. The residue left after the distillation of fraction (*b*) was chromatographed on alumina. Elution with hexane gave twenty-four fractions. The ultraviolet spectrum of

[21] Landolt and Jahn, *Z. phys. Chem.*, 1892, **10**, 303.
[22] Napier and Rodda, *Chem. and Ind.*, 1958, 1319.

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fractions 12—18 showed the presence of biphenyl. Recrystallisation of the combined fractions from ethanol gave biphenyl, m. p. and mixed m. p. 56—57° (Found: relative molar activity × 10^{-2}, 0·94 ± 0·11).

Phenanthrene. The crude phenanthrene from fractions 11—22 of the original chromatogram was recrystallised from ethanol and then rechromatographed on alumina. Further chromatography on partially acetylated cellulose, followed by fractional sublimation, gave phenanthrene, m. p. 96—98°. The fluorescence spectrum of this material suggested that the small amount of impurity may have been 9,10-dihydrophenanthrene. Formation of the picrate, and recrystallisation, followed by chromatography on alumina to decompose the complex, gave phenanthrene, m. p. 98—99° (Found: relative molar activity × 10^{-2}, 22·0 ± 0·21, 1*C requires 20·8).

Anthracene. The ultraviolet and fluorescence spectra of fractions 23—26 showed the presence of a considerable proportion of anthracene together with some phenanthrene and pyrene. Oxidation was carried out in boiling ethanol (10 ml.) with nitric acid (0·2 g.) for 1½ hr. The orange-yellow product was recrystallised from benzene–ethanol (1 : 2). Sublimation under a high vacuum removed traces of the orange phenanthraquinone, leaving a residue of pale yellow 9,10-anthraquinone (5 mg.), m. p. 282—285° (Leitz hot-stage microscope). The sample was diluted with inactive 9,10-anthraquinone (20 mg.) for radiochemical analysis (Found: relative molar activity × 10^{-2}, 21·4 ± 0·21; 1*C requires 20·8).

Pyrene. The mother-liquor from which the crude anthraquinone crystallised was combined with fractions 27—30. (Ultraviolet spectroscopy showed the presence of pyrene in both fractions.) The residue after removal of the solvent was taken up in a few ml. of nitrobenzene, brominated by the addition of a few drops of bromine, and boiled for 2—3 min. The bromo-compound which crystallised on cooling was recrystallised three times from nitrobenzene (the first with a small amount of charcoal) to give 3,5,8,10-tetrabromopyrene (17 mg.), m. p. and mixed m. p. 400—402°. The sample was diluted with an equal amount of inactive material for radiochemical assay (Found: relative molar activity × 10^{-2}, 50·0 ± 0·27; 2·5*C requires 52·0). A second run gave tetrabromopyrene (28 mg.) which was assayed undiluted (Found: relative molar activity × 10^{-2}, 55·2 ± 0·10).

Chrysene. After removal of the solvent from fractions 51—55 the pale yellow residue was recrystallised twice from ethanol, to give chrysene, m. p. 250—251°. This was diluted with twice its weight of inactive chrysene for radiochemical assay (Found: relative molar activity × 10^{-2}, 65·3 ± 0·08; 3*C requires 62·4).

3,4-Benzofluoranthene. Fractions 55—56 and 66—69 were (each set) chromatographed on columns of partially acetylated cellulose. The fractions were examined by ultraviolet spectroscopy, and those fractions containing almost pure 3,4-benzofluoranthene combined and recrystallised from ethanol. Further recrystallisation gave 3,4-benzofluoranthene (9 mg.), m. p. 164—165°. This was diluted with inactive 3,4-benzofluoranthene (18 mg.) for radiochemical analysis (Found: relative molar activity × 10^{-2}, 19·0 ± 0·13; 1*C requires 20·8).

Other products. Attempted purification of 1,2-benzanthracene (from fractions 49—55) and 3,4-benzopyrene (from fractions 56—65 and 66—69) gave products neither sufficiently pure nor in sufficient quantity for radiochemical analysis.

Degradation of Phenanthrene.—Oxidation.[23] To phenanthrene (0·75 g.), isolated from the pyrolysis, were added glacial acetic acid (6·6 g.) and 50% hydrogen peroxide (2·1 g.). The bath-temperature was raised to 110°, whereupon the reaction commenced. After 45 min., the mixture was refluxed for 15 min. The warm solution was poured into an equal volume of water and basified with 25%sodium hydroxide solution (which was added with stirring and warming). After cooling, a small amount of resin was removed. The mixture was warmed (charcoal), filtered, and acidified with hydrochloric acid. Extraction with ether for 6 hr. in a continuous extractor, removal of the solvent, and recrystallisation of the product from water gave 2,2′-biphenic acid, m. p. 225—227°.

Decarboxylation. A mixture of 2,2′-biphenic acid (0·16 g.), copper bronze (0·08 g.), and pure quinoline (7 ml.) was refluxed for 2 hr. The carbon dioxide evolved was led from the top of the condenser and bubbled through a 4% solution of barium hydroxide in a 2-neck flask protected by a potassium hydroxide tube. The whole apparatus was initially swept with dry carbon dioxide-free nitrogen. The barium carbonate was collected for radiochemical assay (Found: relative molar activity × 10^{-2}, 22·3 ± 0·12; 1*C requires 20·8). The products

[23] O'Connor and Moriconi, *Ind. Eng. Chem.*, 1953, **45**, 277.

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were treated with ether (50 ml.) and the filtered solution was extracted with concentrated hydrochloric acid. The aqueous layer was extracted with further portions of ether (2 × 25 ml.), and the combined extracts were washed with 10% hydrochloric acid, 10% sodium hydroxide solution, and water. After drying ($CaCl_2$), the solvent was removed and the residue recrystallised from ethanol–water, to give biphenyl, m. p. 69—70°. The sample was diluted with an equal amount of inactive biphenyl and submitted to radiochemical assay [Found: relative molar activity × 10^{-2}, 1·36 ± 0·02).

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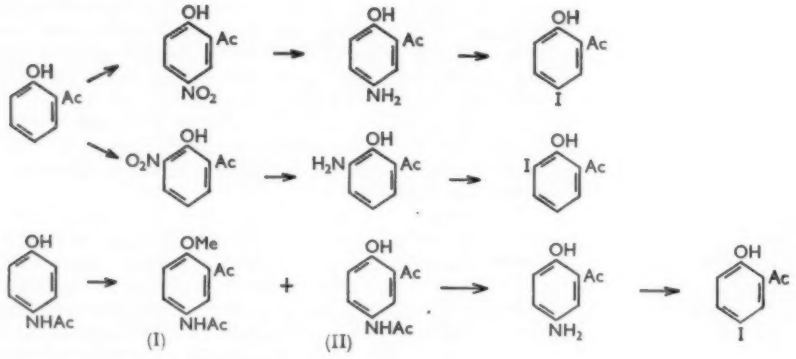
664. *Synthesis of 6-Halogenoflavones and Related Compounds.*

By C. T. CHANG, F. C. CHEN, T. S. CHEN, K. K. HSU, T. UENG, and (MISS) M. HUNG.

Preparation of several new 6-halogeno-flavones, -flavanones, and -flavonols, and corresponding chalcones is described. The nitration of *o*-hydroxyacetophenone and the Friedel–Crafts reaction of *N*-acetyl-*p*-anisidine, expected to yield the acetophenone required as the starting material for the synthesis of 6-iodo-compounds, have been investigated.

IN continuation of previous studies on the halogenoflavones,[1] further compounds were synthesized several years ago.[2-5] 6-Fluoro-,[6] 6-chloro-,[7] and 6-bromo-flavone[8] were prepared in good yield in the usual way from 2-hydroxy-5-halogenoacetophenones which were obtained by Fries rearrangement of *p*-halogenophenyl acetates. However, later, in this Laboratory,[4] attempts to prepare 2-hydroxy-5-iodoacetophenone by this method gave mainly 2,4-di-iodophenol.[9] The iodoacetophenones have now been obtained by the two routes shown in the charts.



[1] Chen and Chang, *J.*, 1958, 146.
[2] F. Chen, D.Sc. Dissertation, 1949, Tôhoku Univ., Sendai, Japan; Chen and Yang, *J. Taiwan Pharm. Assoc.*, 1951, **3**, 39.
[3] Chen and Chang, *J. Formosan Sci.*, 1954, **8**, 74; Chen and Shu, *J. Taiwan Pharm. Assoc.*, 1953, **5**, 49.
[4] T. S. Chen, B.Sc. Thesis, 1956, Nat. Taiwan Univ., Formosa.
[5] Chen, Chang, and Chen, *J. Formosan Sci.*, 1958, **12**, 151; 1959, **13**, 94.
[6] Chen, Chang, Hsu, and Lin, *J. Formosan Sci.*, 1954, **8**, 23.
[7] Chen and Hsu, *J. Formosan Sci.*, 1953, **7**, 51.
[8] Chen, Lai, and Hsieh, *J. Formosan Sci.*, 1953, **7**, 57.
[9] Chang and Chen, *J. Chinese Chem. Soc.*, Series II, 1960, **7**, 69.

The Friedel–Crafts reaction of *N*-acetyl-*p*-anisidine with acetyl chloride in carbon disulphide at 25° afforded 83% of 2-methoxy-5- (I) and only 4% of 2-hydroxy-5-acetamidoacetophenone (II), but at 90° these proportions were reversed.

The 2-hydroxy-5-halogenoacetophenones condensed smoothly with benzaldehyde or *p*-anisaldehyde in presence of alcoholic alkali, giving chalcones, which were cyclized in phosphoric acid to 6-halogenoflavanones. These were easily dehydrogenated by *N*-bromosuccinimide to 6-halogenoflavones, which were also obtained by direct oxidation of the chalcones by selenium dioxide in pentyl alcohol.[10] The 6-halogenoflavonols [3b] were prepared in good yield by cold alkaline hydrogen peroxide.[11,12] When this present work was complete,[5,13] we noted the synthesis of 6-iodoflavone and related compounds in other laboratories.[14]

Experimental

M. p.s were determined in capillary tubes and are uncorrected. Ethanol was used for crystallisation otherwise stated. Microanalyses were made by Mr. E. Aoyagi, Miike Branch, Mitsui Chemical Laboratory, Ohmuda, Japan.

2-Hydroxy-5-fluoro-, -chloro-, and -bromo-acetophenone.—*p*-Fluoro-, *p*-chloro-, and *p*-bromophenyl acetates were treated with anhydrous aluminium chloride, yielding colourless acetophenones as shown in Table 1.

2-Hydroxy-5-iodoacetophenone.—*Method* I. Nitration of *o*-hydroxyacetophenone by the procedure of Allan and Loudon [15] gave steam-volatile 2-hydroxy-5-nitroacetophenone, m. p.

Table 1. *Fries rearrangement of* p-*halogenophenyl acetates to 2-hydroxy-5-halogenoacetophenones.*

p-Halogenophenyl acetate	$AlCl_3$ (g.)	Temp.	Time (hr.)	Product: Yield (%)	Product: M. p. (lit.)
F 30 g.	45	150°	1	88	57—58 (62%, 56—56·5° [a])
Cl 30 g.	45	120	1	70	53—54 (52—54%,[b] 54,[c] 55,[d] 57 [e])
Br 30 g.	45	110	1	50	59—60 (57%,[f] 61—62 [g])

[a] Suter, Lawson, and Smith, *J. Amer. Chem. Soc.*, 1939, **61**, 161. [b] Karrer, Yen, and Reichstein, *Helv. Chim. Acta*, 1930, **13**, 1315. [c] Claus, D.R.-P. 96,659. [d] Auwers and Wittig, *Ber.*, 1924, **57**, 1275. [e] Nencki and Stoeber, *ibid.*, 1897, **30**, 1768. [f] Klarmann, Gates, Shternov, and Cox, *J. Amer. Chem. Soc.*, 1933, **55**, 4657. [g] Feuerstein and Kostanecki, *Ber.*, 1898, **31**, 716, 2953.

Table 2. *2′-Hydroxy-5′-halogenochalcones and the 4-methoxy-compounds.*

2′-Hydroxychalcone *	M. p.	Yield (%)	Found (%): C	H	Hal	Formula	Required (%): C	H	Hal
5′-F	103—104°	83	74·15	4·89	—	$C_{15}H_{11}FO_2$	74·4	4·6	7·9
5′-Cl	111—112 [h]	90	—	—	13·8	$C_{15}H_{11}ClO_2$	69·6	4·3	13·7
5′-Br	109·5—110 [i]	92	59·4	3·8	26·4	$C_{15}H_{11}BrO_2$	59·4	3·7	26·4
5′-I	107—108 [j]	86	51·2	3·3	35·5	$C_{15}H_{11}IO_2$	51·5	3·2	36·2
5-F-4-MeO	125—126	74	77·15	4·9	—	$C_{16}H_{13}FO_3$	70·6	4·8	7·0
5′-Cl-4-MeO	111—112	71	66·2	4·9	12·1	$C_{16}H_{13}ClO_3$	66·6	4·5	12·3
5′-Br-4-MeO	115—116	90	57·55	4·1	23·8	$C_{16}H_{12}BrO_3$	57·7	3·9	24·0
5′-I-4-MeO	130	70	50·45	3·75	33·6	$C_{16}H_{12}IO_3$	50·6	3·5	33·4

* All yellow needles. [h] Ref. *b* of Table I gives m. p. 108°; Kinckell (*Ber.*, 1911, **44**, 3654) gives m. p. 109—110°. [i] Kostanecki and Ludwig (*Ber.*, 1898, **31**, 2951) give m. p. 107—108°. [j] Lit.,[14] m. p. 138°.

101—102° (29%) (lit.,[15] 98—99°, 19%), and involatile 2-hydroxy-3-nitroacetophenone, m. p. 84—84·5° (1·9%) (lit.,[15] 82—83°, 1·9%), which were reduced with stannous chloride and hydrochloric acid, yielding 5-amino-2-, m. p. 112—113° (Found: C, 63·0; H, 6·4; N, 9·1. $C_8H_9O_2N$ requires C, 63·6; H, 6·0; N, 9·3%), and *3-amino-2-hydroxyacetophenone*, m. p. 93—94° (Found: C,

[10] Mahal, Rai, and Venkataraman, *J.*, 1935, 866; 1936, 569.
[11] Algar and Flynn, *Proc. Roy. Irish Acad.*, 1934, **42**, *B*, 1.
[12] Oyamada, *J. Chem. Soc. Japan*, 1934, **55**, 1256.
[13] Chen, Chang, Hung, Lin, and Choong, *Proc. Chem. Soc.*, 1959, 232.
[14] Mulchandani and Shah, *Chem. Ber.*, 1960, **93**, 1913.
[15] Allan and Loudon, *J.*, 1949, 821.

63·2; H, 6·3; N, 9·2%), all yellow needles. Diazotisation, etc., then yielded 2-hydroxy-5- (75%), m. p. 90—91° (lit.,[14] 90°) (Found: C, 37·1; H, 2·9; I, 50·1. Calc. for $C_9H_7IO_2$: C, 36·5; H, 2·7; I, 48·4%), and 2-hydroxy-3-iodoacetophenone (50%), m. p. 58—59° (Found: C, 36·22; H, 2·91; I, 48·2%), both as colourless needles.

Method II. (a) *Acetylation at* 80—90°. To a solution of *N*-acetyl-*p*-anisidine (20 g.) and acetyl chloride (25 c.c.) in dry carbon disulphide (50 c.c.) was added anhydrous aluminium chloride (55 g.) in portions, with stirring, and the mixture was kept at 80—90° for 1·5 hr., while

TABLE 3. *6-Halogenoflavanones and the 4′-methoxy-compounds.*

Flavanone *	M. p.	Yield (%)	Found (%) C	H	Hal	Formula	Required (%) C	H	Hal
6-Fl	77—78°	70	74·1	4·9	—	$C_{15}H_{11}FO_2$	74·4	4·6	7·9
6-Cl- †	96—97	50	—	—	13·9	$C_{15}H_{11}ClO_2$	69·6	4·3	13·7
6-Br	118—119	60	—	—	26·4	$C_{15}H_{11}BrO_2$	59·4	3·7	26·4
6-I	137 [k]	91	51·5	3·4	34·9	$C_{15}H_{11}IO_2$	51·5	3·2	36·2
6-F-4′-MeO	88—89	50	70·2	5·0	—	$C_{16}H_{13}FO_3$	70·6	4·8	7·0
6-Cl-4′-MeO	106—106·5	45	66·4	4·7	12·15	$C_{16}H_{12}ClO_3$	66·6	4·5	12·3
6-Br-4′-MeO	111·5—112·5	40	57·3	4·2	23·8	$C_{16}H_{13}BrO_3$	57·7	3·9	24·0
6-I-4′-MeO	112 [l]	58	50·4	3·9	33·2	$C_{16}H_{13}IO_3$	50·6	3·5	33·4

† Prisms; previously reported by Karrer, Yen, and Reichstein (*Helv. Chim. Acta*, 1930, **13**, 1315) who give no m. p. [k] Lit.,[14] m. p. 136°. [l] Lit.,[14] m. p. 101°.

TABLE 4. *6-Halogenoflavones and the 4′-methoxy-compounds.*

Flavone *	M. p.	Yield [q] (%)	Found (%) C	H	Hal	Formula	Required (%) C	H	Hal
6-F	128—129°	53	74·8	4·0		$C_{15}H_9FO_2$	75·0	3·8	7·9
6-Cl	182—183 [m]	61	—	—	13·9	$C_{15}H_9ClO_2$	70·2	3·5	13·8
6-Br	189—190 [n]	42	—	—	26·5	$C_{15}H_9BrO_2$	59·8	3·0	26·5
6-I	190—191 [o]	74 [p]	51·7	2·9	36·4	$C_{15}H_9IO_2$	51·8	2·6	36·5
6-F-4′-MeO	159—160	50	70·6	4·8	—	$C_{16}H_{11}FO_3$	71·1	4·1	7·0
6-Cl-4′-MeO	180—181	77	66·9	4·1	12·3	$C_{16}H_{11}ClO_3$	67·0	3·9	12·4
6-Br-4′-MeO	192—193	76	57·9	3·7	23·9	$C_{16}H_{11}BrO_3$	58·0	3·4	24·1
6-I-4′-MeO	183	71	50·7	3·2	33·3	$C_{16}H_{11}IO_3$	50·8	2·9	33·6

* Colourless needles. [m] Wittig, Bangert, and Richter (*Annalen*, 1925, **446**, 155) give m. p. 181°; Ruheman (*Ber.*, 1921, **54**, 912) gives m. p. 183—184°. [n] Ref. *i* of Table 2 gives m. p. 189—190°; Bhagwat and Wheeler (*J.*, 1939, 96) give m. p. 192—193°. [o] Lit.,[14] m. p. 184°. [p] Lit.,[14] m. p. 167°. [q] All obtained by the selenium dioxide method; the last compound was also prepared in 55% yield by the *N*-bromosuccinimide method.

carbon disulphide was distilled off. After decomposition with ice-water, the product was collected and extracted with 5% aqueous sodium hydroxide. After acidification of the alkaline solution with hydrochloric acid, the precipitated 5-acetamido-2-hydroxyacetophenone (II) was collected and crystallised as pale yellowish crystals (19·2 g., 82%), m. p. 167—168° (lit.,[16] 165°).

The alkali-insoluble product was recrystallised, giving 5-acetamido-2-methoxyacetophenone (0·7 g., 3%), m. p. 189—190° (lit.,[16] 186—188°).

(b) *Acetylation at* 25°. *N*-Acetyl-*p*-anisidine (20 g.) was treated as above but at 20—25° for 12 hr., then worked up as above, yielding 5-acetamido-2-hydroxyacetophenone (I) (1 g., 4%) and 5-acetamido-2-methoxyacetophenone (II) (20·5 g., 83%).

5-Acetamido-2-methoxyacetophenone (II, 5 g.), anhydrous aluminium chloride (5 g.), and chlorobenzene (25 c.c.) were boiled for 1 hr., then decomposed with ice-water. The chlorobenzene was steam-distilled off, and the precipitate was collected and extracted with 10% aqueous sodium hydroxide. The precipitate formed from the alkaline solution on acidification was collected and crystallised, giving 5-acetamido-2-hydroxyacetophenone (II) (4·3 g., 90%).

5-Amino-2-hydroxyacetophenone.—5-Acetamido-2-hydroxyacetophenone (II) (20 g.) was boiled with 15% hydrochloric acid (25 c.c.) for 40 min., then neutralized with aqueous ammonia and crystallized from 10% ethanol, affording *5-amino-2-hydroxyacetophenone* (13·2 g., 84%), yellow needles, m. p. 112—113° (Found: C, 63·0; H, 6·4; N, 9·1. $C_8H_9O_2N$ requires C, 63·6; H, 6·0; N, 9·3%); its hydrochloride formed colourless plates, m. p. 230—240° (decomp.) (lit.,[14] 118°).

[16] Mathieson and Newberry, *J.*, 1949, 1135.

2-Hydroxy-5-iodoacetophenone.—5-Amino-2-hydroxyacetophenone (5 g.) and ice (20 g.) in 18N-sulphuric acid (18 c.c.) were treated with sodium nitrite (2·4 g.) in water (4 c.c.). When diazotization was complete, more concentrated sulphuric acid (3 c.c.), cupper powder (0·1 g.), and potassium iodide (6·3 g.) in water (10 c.c.) were added. Then the temperature was slowly

TABLE 5. *6-Halogenoflavonols and the 4′-methoxy-compounds.**

Flavonol †	M. p.	Found (%) C	H	Hal	Formula	Required (%) C	H	Hal	Acetate, m. p.
6-F	163—165°	70·1	3·75	—	$C_{15}H_9FO_3$	70·3	3·5	7·4	
6-Cl	162—163 [r]	66·0	3·55	12·8	$C_{15}H_9ClO_3$	66·1	3·3	13·0	
6-Br	183—184	56·7	3·1	25·0	$C_{15}H_9BrO_3$	56·8	2·9	25·2	143—144°
6-I	191—192 [s]	49·3	2·9	34·5	$C_{15}H_9IO_3$	49·5	2·5	34·9	175—176
6-F-4′-MeO	207—208	66·9	4·25	—	$C_{16}H_{11}FO_4$	67·1	3·9	6·6	
6-Cl-4′-MeO	205—206	63·3	3·9	11·4	$C_{16}H_{11}ClO_4$	63·5	3·7	11·7	160—161
6-Br-4′-MeO	193—194	55·2	3·5	22·7	$C_{16}H_{11}BrO_4$	55·4	3·2	23·0	
6-I-4′-MeO	179—180 [t]	48·7	3·0	32·0	$C_{16}H_{11}IO_4$	48·8	2·8	32·2	187—188

* Preliminary reports; Chen and Shu, *J. Taiwan Pharm. Assoc.*, 1953, **5**, 49. † Yellow needles. [r] Minton and Stephen (*J.*, 1922, **121**, 1598) give m. p. 163°. [s] Lit.,[14] m. p. 194°. [t] Lit.,[14] m. p. 186°.

raised and kept at 65° until no more nitrogen was evolved. Steam-distillation and recrystallization yielded 2-hydroxy-5-iodoacetophenone (7 g., 80%) as colourless needles, m. p. 91—92°, identical with the product obtained by method I.

The 6-halogeno-flavones, -flavanones, -flavonols, and corresponding chalcones were prepared as described in a previous paper,[1] and are listed in Tables 2—5.

The authors express their gratitude to Professors S. Fujise and T. Nozoe, Tôhoku University, Japan, for their interest and to Dr. C. H. Yang, Mr. C. K. Chang, and Miss L. S. Wang for experimental assistance. Financial support from the Asia Foundation and the National Council on Science Development, as well as encouragement from President S. L. Chien and Professor E. Sebe, are greatly appreciated.

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665. *Co-ordination Compounds Formed by Tetrafluorides of the Sulphur Sub-group.*

By NEIL BARTLETT and P. L. ROBINSON.

Fluoride ion acceptors form co-ordination compounds with the tetrafluorides of Group VIB elements. The sulphur compounds can be converted easily into their selenium analogues. These conversions are useful for the convenient generation of sulphur tetrafluoride and its purification. The nature of the bonding in the adducts is discussed.

IN a preliminary communication,[1] we described new co-ordination compounds formed by the tetrafluorides of sulphur, selenium, and tellurium. Sulphur tetrafluoride complexes are convertible into selenium analogues by displacement of the more volatile base and we have outlined a method [2] of purifying sulphur tetrafluoride, based on this. The recent development of a convenient preparative method [3] for sulphur tetrafluoride and the demonstration of its synthetic value as a fluorinating agent [4] has stimulated further interest in its derivatives.

Sulphur tetrafluoride, mixed with thionyl fluoride or other sulphur fluorides, can easily be isolated by first making the boron trifluoride adduct, SF_4,BF_3, from which the other

[1] Bartlett and Robinson, *Chem. and Ind.*, 1956, 1351.
[2] Bartlett and Robinson, *Proc. Chem. Soc.*, 1957, 230.
[3] Tullock, Fawcett, Smith, and Coffman, *J. Amer. Chem. Soc.*, 1960, **82**, 539.
[4] Hasek, Smith, and Engelhardt, *J. Amer. Chem. Soc.*, p. 543; Smith, Tullock, Smith, and Engelhardt, *ibid.*, p. 551.

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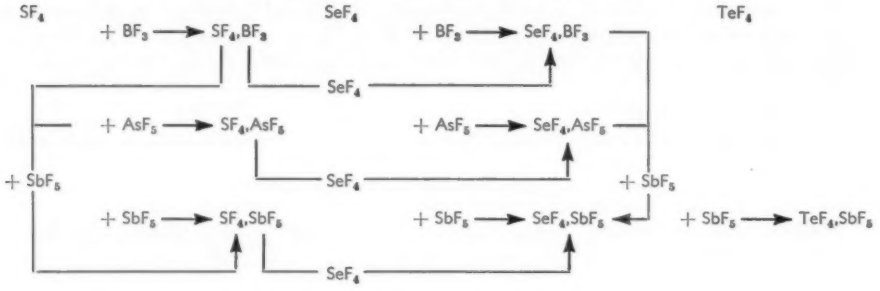
fluorides can readily be removed. This compound is also formed when boron–sulphur mixtures are fluorinated at low temperatures and when sulphur tetrafluoride fluorinates borosilicate glass. In the latter reaction, which occurs above 300°, the formation of the adduct is accompanied by deposition of sulphur, probably produced in the disproportionation $3SF_4 \longrightarrow 2SF_6 + S$. Boron trifluoride is formed in the reaction $6SF_4 + 2B_2O_3 \longrightarrow 4BF_3 + 6SOF_2$.

The arsenic pentafluoride complex, SF_4,AsF_5, which is much less volatile than SF_4,BF_3, can be stored indefinitely in Pyrex glass ampoules, as can the antimony pentafluoride complex; this is, however, more troublesome to prepare. Selenium tetrafluoride will displace sulphur tetrafluoride from all these complexes: $SeF_4 + SF_4,A \longrightarrow SeF_4,A + SF_4$. It is probable that other basic liquid fluorides such as arsenic trifluoride, iodine pentafluoride, and bromine trifluoride will also liberate sulphur tetrafluoride from its adducts. Boron trifluoride can be removed from SF_4,BF_3 by passing the vapour over sodium fluoride at 240°: $SF_4,BF_3 + NaF \longrightarrow SF_4 + NaBF_4$. But this is a less convenient and efficient preparative method for sulphur tetrafluoride than displacement with liquid bases.

The more volatile acid can also be displaced by a less volatile one, so that boron trifluoride and arsenic pentafluoride complexes can be converted by antimony pentafluoride into SF_4,SbF_5 and SeF_4,SbF_5. The former is more easily prepared in this way

Inter-relationships between the complexes of SF_4, SeF_4, *and* TeF_4.



than by direct combination. Interconversions which can easily be made are shown schematically.

Neither sulphur tetrafluoride nor selenium tetrafluoride forms a co-ordination complex with platinum dichloride; this indicates that they are unlikely to be electron-pair donors. It is significant that phosphorus trifluoride, although it forms a co-ordination complex with platinum dichloride involving donation of the phosphorus "lone pair," [5] does not combine with boron trifluoride.[6]

The adduct SF_4,BF_3 is completely dissociated in the vapour phase and the enthalpy of dissociation is consistent with the ionic formulation $SF_3^+BF_4^-$. Table 1 gives present thermodynamic data for the adduct together with the values of Cotton and George [7] and Seel and Detmer; [8] enthalpies of dissociation of other boron trifluoride derivatives (cf. ref. 9) are included for comparison. The enthalpy of formation for the arsenic pentafluoride adduct is greater than for SF_4,BF_3.

Nuclear magnetic resonance measurements by Cotton and George [10] and by Muetterties

[5] Chatt and Williams, *J.*, 1951, 3061.
[6] Booth and Walkup, *J. Amer. Chem. Soc.*, 1943, **65**, 2334.
[7] Cotton and George, *J. Inorg. Nuclear Chem.*, 1960, **12**, 386.
[8] Seel and Detmer, *Z. anorg. Chem.*, 1959, **301**, 113.
[9] Greenwood and Martin, *Quart. Rev.*, 1954, **8**, 1.
[10] Cotton and George, *J. Inorg. Nuclear Chem.*, 1958, **7**, 397.

and his co-workers [11] indicate that the bonding in SF_4,BF_3 is either ionic or by fluorine bridging. It is evident, however, that sulphur tetrafluoride is a poor acceptor since it does not combine with nitryl fluoride [12] or with cæsium fluoride. The tendency, therefore, for the sulphur atom to attain a pseudo-octahedral co-ordination, such as it would have

TABLE 1.

Compound	van't Hoff equation	Enthp. of dissn. (kcal. mole^{-1})	Reference
SF_4,BF_3	$\log p_{mm.} = 12{\cdot}8 - 3230/T$	29·6	7
SF_4,BF_3	$\log p_{mm.} = 11{\cdot}34 - 2783/T$	25·5	8
SF_4,BF_3	$\log p_{mm.} = 11{\cdot}11 - 2716/T$	24·8 ± 0·2	Present work
$CsBF_4$		26·9	9
$RbBF_4$		27·0	9
KBF_4		28·9	
SF_4,AsF_5	$\log p_{mm.} = 10{\cdot}26 - 3376/T$	31·0 ± 0·8	Present work

in the bridged structure, must be small; and the pseudo-tetrahedral co-ordination of the SF_3^+ ion may well be preferred. Possibly fluorine bridging may be more important in selenium tetrafluoride derivatives since this tetrafluoride can act as a fluoride ion acceptor to form the SeF_5^- ion [13] in which the selenium is presumed to attain a pseudo-octahedral co-ordination.

X-Ray powder photographs of the sulphur tetrafluoride derivatives are simpler than those of their selenium analogues. The pattern of SF_4,SbF_5 only has been indexed; in the simple cubic unit cell, $a = 5{\cdot}625 \pm 0{\cdot}002$ Å, there is one molecule. The structure determination has not been completed, but the symmetry is suggestive of an ionic formulation $SF_3^+SbF_6^-$.

Enhancement of the electrical conductivity of selenium tetrafluoride by antimony pentafluoride indicates considerable ionisation of the complex: $SeF_4,SbF_5 \longrightarrow SeF_3^+ + SbF_6^-$.

When a mixture of potassium chloride with the adduct SeF_4,SbF_5 is heated in a vacuum, a volatile, thermally unstable product is obtained which rearranges to a mixture of the tetrafluoride and tetrachloride of selenium. It is probable that this initial product, which is a pale yellow liquid, may be selenium trifluorochloride:

$$SeF_3,SbF_6 + KCl \longrightarrow SeF_3Cl + KSbF_6;\ 4SeF_3Cl \longrightarrow 3SeF_4 + SeCl_4$$

Selenium tetrafluoride derivatives of platinum tetrafluoride, $(SeF_4)_2PtF_4$ [previously given [14] as $(SeF_4)_2PtF_2$] and of gold trifluoride, SeF_4,AuF_3, are thermally more stable than the bromine trifluoride acids $(BrF_3)_2PtF_4$ [15] and BrF_3,AuF_3,[16] from which they are derived by displacement of the bromine trifluoride with an excess of selenium tetrafluoride. Selenium tetrafluoride and bromine trifluoride do not react in the liquid phase.

$$(BrF_3)_2PtF_4 + 2SeF_4 \longrightarrow (SeF_4)_2PtF_4 + 2BrF_3$$
$$BrF_3,AuF_3 + SeF_4 \longrightarrow SeF_4,AuF_3 + BrF_3$$

High-temperature decomposition of these complexes gives rise to platinum and gold since the selenium tetrafluoride acts as a reducing agent:

$$(SeF_4)_2PtF_4 = 2SeF_6 + Pt\ (350°)$$
$$3SeF_4,AuF_3 = AuF_3 + 2Au + 3SeF_6\ (350°)$$

Bartlett, Lohmann, and Quail [17] have shown that the platinum adduct $(SeF_4)_2PtF_4$ is isomorphous with the complexes $(SeF_4)_2GeF_4$ and $(SeF_4)_2PdF_4$.

[11] Oppegard, Smith, Muetterties, and Engelhardt, *J. Amer. Chem. Soc.*, 1960, **82**, 3836.
[12] Hetherington, Ph.D. Thesis, Durham, 1955.
[13] Aynsley, Peacock, and Robinson, *J.*, 1952, 1231.
[14] Hair and Robinson, *J.*, 1960, 3419.
[15] Sharpe, *J.*, 1950 3444.
[16] Sharpe, *J.*, 1949, 2901.
[17] Bartlett, Lohmann, and Quail, unpublished work.

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It has not been possible to isolate sulphur and tellurium analogues of $(SeF_4)_2PtF_4$ and SeF_4,AuF_3. The pale pink solid, formed when ruthenium pentafluoride is mixed with sulphur tetrafluoride, is probably SF_4,RuF_5 which would be analogous to SF_4,OsF_5 and SF_4,IrF_5, but a ruthenium pentafluoride analogue of SeF_4,OsF_5 and SeF_4,IrF_5 [18] cannot be isolated, although the ruthenium and selenium fluorides are miscible.

The higher melting point of tellurium tetrafluoride prevents the preparation of boron trifluoride and arsenic pentafluoride derivatives by direct addition; but antimony pentafluoride dissolves the tetrafluoride, and removal of the solvent leaves TeF_4,SbF_5. In contrast to the sulphur and selenium analogues and unlike antimony pentafluoride itself, hydrolysis of this adduct is slow, although exothermal, and is accompanied by the precipitation of tellurium dioxide: $TeF_4,SbF_5 + 2H_2O \longrightarrow TeO_2 + H^+ + SbF_6^- + 3HF$. Although this could be interpreted as indicative of an ionic formulation, there is no structural evidence on the point. The *X*-ray powder pattern was not indexed.

Boron trichloride does not form adducts with the sulphur or selenium tetrafluorides but interacts very energetically thus:

$$3SF_4 + 4BCl_3 \longrightarrow 3SCl_2 + 3Cl_2 + 4BF_3$$
$$3SeF_4 + 4BCl_3 \longrightarrow 3SeCl_4 + 4BF_3$$

Experimental

Purification of Sulphur Tetrafluoride.—(*a*) Sulphur tetrafluoride, made as described by Brown and Robinson [19] and containing silicon tetrafluoride and other fluorides of sulphur, was mixed at ~−180° with an equal bulk of boron trifluoride. The excess of boron trifluoride, sulphur hexafluoride, thionyl fluoride, and other sulphur fluorides was removed at −75° under a vacuum. The adduct SF_4,BF_3 remained. Selenium tetrafluoride, prepared as described by Aynsley, Peacock, and Robinson,[13] was distilled under a vacuum on to the SF_4,BF_3; on warming to room temperature the mixture evolved sulphur tetrafluoride. The gaseous product was passed through a Podbielniak fractionation column, all distilling at −40·4°/1 atm., the b. p. for the pure tetrafluoride.[19] Vapour-density measurements indicated $M = 108{\cdot}9 \pm 1{\cdot}0$ (Calc. for SF_4: $M = 108{\cdot}1$).

When too little selenium tetrafluoride to displace the sulphur tetrafluoride was used, SeF_4,BF_3, m. p. 50°, remained after the excess of SF_4,BF_3 had been removed at 20° under a vacuum.

(*b*) We are indebted to a Referee for suggesting that the reaction of SF_4,BF_3 with ethyl ether mentioned on p. 3422 was probably $SF_4,BF_3 + Et_2O \longrightarrow Et_2O,BF_3 + SF_4$ and that, if so, then readily accessible ether could be used in place of selenium tetrafluoride in our purification of sulphur tetrafluoride through the SF_4,BF_3 compound. We have found that the reaction goes smoothly when well dried ether is condensed on to SF_4,BF_3 at −190° and the mixture allowed to rise in temperature. A clear liquid is formed which evolves sulphur tetrafluoride. This was condensed at −190° and a specimen of the vapour gave infrared absorption peaks at 728vs, 870vs, 890vs, 1280m cm.$^{-1}$ (cf. 728vs, 867vs, 889vs, 1281m cm.$^{-1}$; ref. 20. The only impurities detected were traces of silicon tetrafluoride and thionyl fluoride which probably arose from moisture on the sodium chloride windows of the cell, since their peaks were weaker on a second filling. Neither boron trifluoride nor sulphur hexafluoride was present.

Preparation of SF_4,BF_3.—(a) SF_4 *with* BF_3. Both sulphur tetrafluoride and boron trifluoride are gases and can be manipulated volumetrically. The volumes were measured in a 1-l. bulb to which were attached a mercury manometer and two condensation limbs, one with a tap. After the pressure of the sulphur tetrafluoride had been measured in the bulb; it was condensed in the limb with the tap, which was then closed. The boron trifluoride was measured in the same way and condensed in the other limb. The sulphur tetrafluoride was condensed on to the boron trifluoride and the mixture allowed to react at about −100°. When the two initial gas pressures were equal the pressure for the product was independent of them. Clearly the vapour pressure or dissociation pressure of the co-ordination

[18] Hepworth, Robinson, and Westland, *Chem. and Ind.*, 1955, 1516.
[19] Brown and Robinson, *J.*, 1955, 3147.
[20] Dodd and Woodward, *Trans. Faraday Soc.*, 1956, **52**, 1055.

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compound was being registered, for an excess of either reactant led to a final pressure greater than this. Whatever the proportions, however, the properties of the solid were always the same, and it was concluded that one co-ordination compound only is formed, namely SF_4,BF_3. Typical results from equimolar proportions at 19° were:

Pressure of each gas (mm.)	206	285	410
Pressure of compound (mm.)	99	107	110

(b) *Fluorination of boron–sulphur mixtures.* Fluorination at room temperatures failed to produce the adduct, even with dilute fluorine. At −75°, however, a mixture of 95—97% boron and sulphur gave SF_4,BF_3 which slowly crystallised on the walls of the vessel. This sublimed at ~60° and qualitative tests confirmed its nature.

(c) *Fluorination of borosilicate glass with* SF_4. Reaction did not occur until ~350°; the heating flame was then coloured by the hot glass and there was marked etching. Sulphur was deposited just beyond the hot zone and, further away, acicular white crystals of SF_4,BF_3. Some sulphur hexafluoride was also formed.

Dissociation Pressure of SF_4,BF_3.—Vapour pressures were measured with a simple isoteniscope to which a tap-bottle containing freshly prepared material could be attached. This was of exaggerated wine-bottle form, to give minimum volume with maximum surface exposed to the bath liquid and to shorten the time required for thermal equilibrium. Its tap was spring-loaded to prevent seepage of water when, at higher temperatures, the grease had softened a little. It was connected to one side of the small differential mercury gauge by an A10 cone-and-socket joint secured by lugs and springs. This side of the gauge could be evacuated through a tap to a vacuum-line, and the other was connected to a mercury manometer and, by a two-way tap, separately to the vacuum-line and a fine capillary. The arrangement was sufficiently small to allow the bottle, the tap to the vacuum line, and the differential gauge to be submerged in water in a 5-l. beaker. All joints and taps were lubricated with stiff fluorocarbon grease. Manometer levels were measured with a cathetometer. The dissociation pressure increased as the material approached the working temperature and was balanced by admitting air through the capillary. Sufficient pressure–temperature readings were taken to ensure reliable results (Table 2). Between measurements the material was cooled at −75° and the apparatus was evacuated.

TABLE 2.

Temp. (K)	273·2°	291·2°	294·2°	298·2°	301·2°	303·2°	308·2°	311·2°	313·2°	314·2°
Pressure (mm.)	20	59	74	94	119	133	187	237	291	295
Temp. (K)	317·2°	319·2°	321·2°	323·2°	324·2°	326·2°	327·2°	329·2°	330·2°	
Pressure (mm.)	340	401	437	478	534	589	647	692	755	

Vapour Density of SF_4,BF_3.—A thin-walled glass bulb of about 50 c.c. capacity was filled with gaseous SF_4,BF_3 in equilibrium with the solid. Its volume was found by weighing the bulb full of water. Measurements were made at 39·5° and 19·5° (Table 3). Clearly the pressures are the dissociation pressures of SF_4,BF_3 which dissociates thus: $s \longrightarrow g + g$, so that $K_p = \frac{1}{4}(P_{atm.})^2$.

TABLE 3.

Temp. (°C)	Observed density	Calc. density for a 1 : 1 mixture of SF_4 and BF_3	Calc. density for SF_4,BF_3
39·5°	44·1	43·7	87·5
19·5	43·1	43·7	87·5

Thermodynamic Data for SF_4,BF_3.—The vapour pressure–temperature measurements can be expressed by:

$$\log_e K_{P_{atm.}} = -\frac{12{\cdot}51 \times 10^3}{T(°K)} + 36{\cdot}50$$

$$\Delta G = 2{\cdot}483 \times 10^4 - 72{\cdot}50T \text{ cal. mole}^{-1}$$

Now $\Delta G = \Delta H - T\Delta S$, so $\Delta H = +24{\cdot}83$ kcal. mole^{-1}, and $\Delta S = 72{\cdot}50$ cal. per degree per mole.

Reactions of SF_4,BF_3.—When the adduct was vaporised in a stream of nitrogen over sodium fluoride at 240—250°, boron trifluoride combined with the salt to give sodium tetrafluoroborate, and sulphur tetrafluoride passed on.

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Water, ethyl alcohol, and ethyl ether reacted vigorously and exothermally with the adduct; the resulting clear aqueous solution reduced permanganate and gave a precipitate with nitron. In carbon tetrachloride, trichloroethylene, carbon disulphide, and liquid sulphur dioxide, the adduct was insoluble. In 100% sulphuric acid, it dissolved with the vigorous evolution of boron trifluoride, and, after considerable additions of the solid, gave acicular white crystals which may have been SF_4,SO_3, analogous to SeF_4,SO_3.[21]

Preparation of SF_4,AsF_5. Arsenic pentafluoride, made by fluorinating "AnalaR" arsenious oxide in a nickel tube, was mixed with sulphur tetrafluoride in the apparatus used in the synthesis of SF_4,BF_3. From equal volumes of the two gases at the same temperature and pressure, the vapour pressure of the product was always very small, and an excess of either increased the final pressure. The evidence suggested that SF_4,AsF_5 was the only compound formed. It was initially white but rapidly became pale blue. Typical results at 19° were:

SF_4	AsF_5	Resultant pressure
1 vol., 138·2 mm.	1 vol., 138·2 mm.	5 mm.
2 vols., 31·7 mm.	1 vol., 31·7 mm.	33 mm.

When residual gas was pumped off, the solid showed a very low vapour pressure at 20°.

Properties. The adduct sublimed when warmed in a vacuum, and the vapour pressure was about an atmosphere at 180°. Vapour pressure–temperature measurements are expressed by $\ln K_{P\,atom} = -(15{\cdot}55 \times 10^3)/T + 32{\cdot}60$. $\Delta H = 31{\cdot}0 \pm 0{\cdot}8$ kcal. mole^{-1}, $\Delta S = 65{\cdot}0$ cal. degree^{-1} mole^{-1}.

Selenium tetrafluoride dissolved the solid, sulphur tetrafluoride being evolved. Removal of the excess of selenium tetrafluoride left the white solid, SeF_4,AsF_5. Water reacted vigorously with the adduct, and the clear solution gave a precipitate of nitron fluoroarsenate with nitron acetate. Hydrogen sulphide precipitated sulphur and, after the solution had been boiled with hydrochloric acid, arsenic sulphide. Ethyl alcohol and ethyl ether reacted vigorously, but the adduct was insoluble in carbon tetrachloride.

Preparation of SF_4,SbF_5.—Antimony pentafluoride, made by Woolf and Greenwood's method,[22] was used to prepare SF_4,SbF_5 in three ways:

(*a*) An excess of sulphur tetrafluoride was condensed on to antimony pentafluoride in a bulb with a break-seal, which was cooled to −180° and sealed under a vacuum. Since antimony pentafluoride is a glass at −40° and viscous even at 20°, the mixture had to be raised to room temperature to secure reaction. Repeatedly the bulb was cooled to −180° and the container was shaken to break up the solid which was formed at the interface between the two fluorides. After two days, when the reaction was judged to be complete, the excess of sulphur tetrafluoride was removed under a vacuum through the break-seal, leaving a white solid, m. p. 245°.

A sample of this product was dissolved in sodium hydroxide, and the antimony determined by acidification with hydrochloric acid, reduction with sulphur dioxide, boiling to remove the excess, and titration with potassium bromate and Methyl Red. Fluorine was precipitated as lead chlorofluoride in the distillate from sulphuric acid at 132—138°; the composition was checked by dissolving the solid *adduct* in dilute nitric acid and precipitating the chloride as silver chloride. Sulphur was precipitated as barium sulphate from a solution oxidised with hydrogen peroxide (Found: Sb, 38·9; S, 9·1; F, 52·1. SF_4,SbF_5 requires Sb, 37·5; S, 9·9; F, 52·6%).

(*b*) It is much more convenient to use the reaction $SbF_5 + SF_4,BF_3 \longrightarrow SF_4,SbF_5 + BF_3$. A deficiency of the former reactant was distilled, under a vacuum, on to the latter, boron trifluoride being displaced as the antimony pentafluoride melted. The excess of SF_4,BF_3 was removed under a vacuum at room temperature, leaving a white residue melting slightly above 240° (Found: Sb, 36·0; F, 52·4%).

(*c*) A reaction similar to the last, but with SF_4,AsF_5, released arsenic pentafluoride and left SF_4,SbF_5.

X-*Ray Powder Photographs of* SF_4,SbF_5.—Thin-walled, 0·5 mm. capillaries were filled with the adduct in a dry box and sealed off with a very small flame. Photographs were taken at 18° ± 2° on a 19 cm. Unicam camera with crystal-reflected Fe-K_α radiation from a lithium fluoride monochromator. The reflexions were indexed on a simple cubic unit cell: $a = 5{\cdot}625 \pm 0{\cdot}002$ Å, $U = 178$ Å^3, $D_n = 3{\cdot}1 \pm 0{\cdot}1$, $Z = 1$, $D_c = 3{\cdot}03$. The density was determined in a

[21] Peacock, *J.*, 1953, 3617.
[22] Woolf and Greenwood, *J.*, 1950, 2200.

1 ml. density bottle with a ground glass cap; this was loaded in a dry box. Carbon tetrachloride was the displacement fluid.

Miscellaneous reactions of SF_4,SbF_5.—Selenium tetrafluoride dissolved it at about 30°, sulphur tetrafluoride being evolved and SeF_4,SbF_5 left. Water reacted vigorously and nitron acetate precipitated nitron fluoroantimonate from the clear solution, but hydrogen sulphide gave only sulphur until the solution had been evaporated with hydrochloric acid; then antimony sulphide could be precipitated.

Other Reactions of Sulphur Tetrafluoride.—Platinum dichloride. Platinous chloride, prepared by heating platinic chloride at 500° in chlorine, reacted readily with phosphorus trifluoride, as described by Chatt and Williams,[5] to give $PtCl_2,2PF_3$, but not at all with sulphur tetrafluoride between −40° and 200°.

Boron trichloride. Equal volumes of boron trichloride and sulphur tetrafluoride were mixed. On warming they reacted violently; a little red liquid and some chlorine were formed. The final pressure at 18° was greater than the sum of the initial pressures and compatible with $4SF_4(g) + 4BCl_3(g) \longrightarrow 4BF_3(g) + 3SCl_2(l) + 3Cl_2(g) + SF_4(g)$; an amount of trichloride necessary to satisfy the reaction $3SF_4(g) + 4BCl_3(g) \longrightarrow 4BF_3(g) + 3SCl_2(l) + 3Cl_2(g)$ led to almost the same final pressure. The respective pressures (mm. at 18°) were:

Pressure of SF_4	60·5	Pressure of SF_4	60·5
Pressure of BCl_3	60·5	Pressure of BCl_3	80·5
Resultant pressure after mixing of equal volumes	146·5	Resultant pressure after mixing of equal volumes	145·7

The red liquid, b. p. 60°, was hydrolysed slowly in water, precipitating sulphur, and was sulphur dichloride (b. p. 59°).

Ruthenium pentafluoride [23] at its m. p. (108°) gave, with sulphur tetrafluoride vapour, a pinkish-white solid which melted with decomposition at 150° to a port-wine-coloured liquid. This lost gas rapidly under a vacuum, reverting to ruthenium pentafluoride. The viscosity of the latter made complete reaction impossible, and the compound was not identified.

Molybdenum hexafluoride,[24] when mixed with sulphur tetrafluoride, gave, at −40° and below, an intensely yellow solid which decomposed above that temperature.

Chlorine did not react with sulphur tetrafluoride at room temperature.

Cæsium fluoride showed no evidence of combination at any temperature between −40° and 220°.

Preparation of SeF_4,BF_3.—Selenium tetrafluoride and a large excess of boron trifluoride were distilled into a trap at −180° and allowed to come to room temperature under dry air. The excess of boron trifluoride was evolved and a white solid, m. p. 50°, remained. It was dissolved in sodium hydroxide, and the selenium determined by reduction with sulphurous acid in hydrochloric acid. Fluoroborate was precipitated from a solution of the *adduct* in a dilute acetic acid, with nitron (Found: Se, 34·9; BF_4^-, 38·5. SeF_4,BF_3 requires Se, 35·9; BF_4^-, 39·0%).

Preparation by the action of selenium tetrafluoride on SF_4,BF_3 is easier.

The adduct melted to a clear liquid at 50° and began to liberate boron trifluoride at 60°. Water decomposed it vigorously; it was freely soluble in ether without evident reaction, but was insoluble in carbon tetrachloride. Antimony pentafluoride displaced boron trifluoride to give SeF_4,SbF_5.

Preparation of SeF_4,AsF_5.—Selenium tetrafluoride was melted with an excess of arsenic pentafluoride under pressure. As the former absorbed the latter it became warm and viscous and granular crystals slowly appeared. Eventually the vessel was warmed and the uncombined selenium tetrafluoride was removed under a vacuum. White crystals, m. p. 118—120°, of the *adduct* remained which evolved a little gas on melting. They were dissolved in sodium hydroxide, and selenium and fluorine were determined. Arsenic was found by titrating the boiled filtrate from the selenium with potassium bromate solution against Methyl Red (Found: Se, 25·1; As, 22·7; F, 48·0. SeF_4,AsF_5 requires Se, 24·3; As, 23·1; F, 52·6%).

Water reacted violently with this product, and the clear solution gave a precipitate of nitron fluoroarsenate with nitron acetate. Antimony pentafluoride displaced arsenic pentafluoride.

[23] Hepworth, Peacock, and Robinson, *J.*, 1954, 1197.

[24] Dodd and Robinson, "Experimental Inorganic Chemistry," Elsevier Publ. Co., Amsterdam, 1954, p. 221.

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Preparation of SeF_4,SbF_5.—Mixing selenium tetrafluoride and antimony pentafluoride produced much heat and large white crystals separated as the liquid cooled. When the excess of tetrafluoride was removed under a vacuum at 120°, the crystals melted sharply at 122° to a colourless liquid. The *product* was stable up to 200° and could be distilled unchanged in a vacuum. It was dissolved in sodium hydroxide and analysed (Found: Se, 21·3; Sb, 32·8; F, 45·9. SeF_4,SbF_5 requires Se, 21·2; Sb, 32·8; F, 46·0%).

The electrical conductivity of a solution of SeF_4,SbF_5 in selenium tetrafluoride was determned in a U-shaped silica cell charged by rotating a trap containing the solution about a cone-and-socket joint. The liquid was received into a reservoir from which some of it could be poured over a weir into the smaller electrode chamber. The resistance between platinum electrodes was measured with a bridge circuit of a modified Kohlrausch type. The resistance remained constant for 15 min. and did not change when the liquid in the electrode chamber was re-mixed with that in the reservoir. All measurements were made at 25° ± 0·01°.

The concentration was found by running the liquid into potassium hydroxide and determining the selenium and antimony; it was 271 g. of antimony pentafluoride per kg. of selenium tetrafluoride, approximately 1 mole per kg. The cell constant was found with a known potassium chloride solution, the specific conductivities of Jones and Bradshaw [25] being employed:

SbF_5,SeF_4 (1 mole/1000 g. of SeF_4), $\kappa = 5{\cdot}6 \times 10^{-3}$ ohm^{-1} cm.$^{-1}$ at 25°.
SbF_5, $\kappa = 1{\cdot}2 \times 10^{-3}$ ohm^{-1} cm.$^{-1}$ at 25° (cf. ref. 22).
SeF_4, $\kappa = \sim 10^{-5}$ ohm^{-1} cm.$^{-1}$ at 25° (cf. ref. 26).
KCl (standard), $\kappa = 0{\cdot}012836$ ohm^{-1} cm.$^{-1}$; resistance 42·4 ohms.
The resistance of the SeF_4–SbF_5 solution was 97·5 ohms.

Preparation of $(SeF_4)_2PtF_4$.—The complex fluoride, $(BrF_3)_2PtF_4$, was prepared as described by Sharpe.[15] When this was warmed with selenium tetrafluoride, bromine trifluoride was evolved and an orange-yellow solid remained in suspension. The mixture was refluxed for some time and the volatile material distilled off under a vacuum. The residual solid showed no evidence of decomposition even at 248° under a vacuum. At about 350° under atmospheric pressure, it decomposed rapidly and left a black residue which an *X*-ray photograph showed to be metallic platinum. The *salt* was decomposed in aqueous sodium hydroxide: a little of the platinum was precipitated as the hydrated dioxide; this was filtered off and ignited to metal. Selenium and fluorine were determined, and the platinum in the boiled filtrate from the selenium was precipitated with zinc [Found: Pt, 32·7; Se, 26·9; F, 39·6. $(SeF_4)_2PtF_4$ requires Pt, 33·6; Se, 27·2; F, 39·2%].

Preparation of SeF_4,AuF_3.—The complex BrF_3,AuF_3, prepared as described by Sharpe,[16] was dissolved in hot selenium tetrafluoride, and the bromine trifluoride was displaced by refluxing. When the solvent was distilled off under a vacuum, a yellow solid remained, from which an *X*-ray photograph showed auric fluoride to be absent. The *adduct* was hydrolysed in moist air to auric hydroxide and dissolved in dilute hydrochloric acid to a clear yellow solution. From this gold and selenium were precipitated with sulphur dioxide. Fluorine was determined on a separate sample decomposed in alkali (Found: Au + Se, 67·5; F, 31·5. SeF_4,AuF_3 requires Au + Se, 67·5; F, 32·5%). When the adduct was heated under atmospheric pressure to 210°, a little selenium tetrafluoride condensed on the cooler parts of the vessel. The residue had become khaki-coloured, but analysis showed that it was still largely unchanged complex. The slight residue from treatment with hydrochloric acid was presumably gold, since it dissolved only in aqua regia. At 350°, however, decomposition to gold was rapid.

Other Reactions of Selenium Tetrafluoride.—Boron trichloride reacted vigorously with an excess of selenium tetrafluoride when the latter melted, liberating boron trifluoride and leaving a cream-coloured solid when this and the excess of boron trichloride were removed under a vacuum. This was sublimable under a vacuum and proved to be selenium tetrachloride (Found: Se, 35·4; Cl, 63·0. Calc. for $SeCl_4$: Se, 35·7; Cl, 64·3%).

Ruthenium pentafluoride gave a green solution in selenium tetrafluoride, from which it was recovered unchanged when the solvent was distilled off at 20° under a vacuum.

Platinum dichloride reacted with neither the liquid tetrafluoride nor its vapour up to 200°.

Preparation of TeF_4,SbF_5.—Tellurium tetrafluoride [27] dissolved in antimony pentafluoride

[25] Jones and Bradshaw, *J. Amer. Chem. Soc.*, 1933, **55**, 1780.
[26] Hub and Robinson, unpublished result.
[27] Campbell and Robinson, *J.*, 1956, 785.

at 40° and a white solid crystallised as the solution cooled. It was recovered by pumping off the solvent at 100°. The *adduct*, m. p. 206°, reacted very quietly with water, tellurium dioxide being precipitated. It was dissolved in potassium hydroxide and the tellurium was precipitated with sulphurous acid and hydrazine hydrate after acidification with hydrochloric acid (Found: Te, 28·5; F, 41·2. TeF_4,SbF_5 requires Te, 30·2; F, 40·7%).

Boron trifluoride did not react with solid or liquid tellurium tetrafluoride.

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666. *A New Calorimeter for Heats of Mixing. The Heat of Mixing of Benzene with Carbon Tetrachloride.*

By J. A. LARKIN and M. L. MCGLASHAN.

A new calorimeter for measuring heats of mixing has been made and tested. It is believed to be capable of higher precision, and to be more convenient, than any previous design. The new calorimeter has been used to make an extensive series of measurements, with a probable error of about $\pm 0{\cdot}3$ J $mole^{-1}$, on benzene + carbon tetrachloride at 25°. The results are about 4 J $mole^{-1}$ higher than was expected after consideration of several sets of previous measurements. It is believed that the discrepancies are due to incomplete mixing to varying degrees in all the previous calorimeters.

WE have made and tested a new calorimeter for measuring the heats of mixing of liquids and believe it to be capable of higher precision, and to be more convenient, than any previous design. The liquids are mixed out of any contact with vapour spaces which, even when they are very small, can lead [1,2] to large errors in measurements of heats of mixing. Completeness of mixing is easily achieved, and can easily be confirmed in the course of an experiment by making use of the fact that when mixing is complete the heat of stirring (stirring in this case by inversion of the mixing vessel) is reproducible. The new calorimeter is an improved version of one tentatively described elsewhere.[3] A troublesome gasket has been eliminated so that the liquids can now be mixed without danger of leakage from the calorimeter (which would of course lead to large errors due to cooling when even an otherwise negligible quantity of liquid evaporated from the surface into the surrounding vacuum), and without the liquids ever coming into contact with gasket material or grease with which they might interact. The arrangement of the calorimeter thermometer has been improved; it now consists of four thermistors connected in parallel and distributed over the surface of the calorimeter.

Several pairs of liquids have been used to prove new calorimeters.[1] The choice of a suitable pair of liquids should be governed by the following criteria: (*a*) they should be easily purified; (*b*) they should be at least as difficult to mix (*e.g.*, they should have widely different densities) as any pair which it is proposed to study in the calorimeter; (*c*) if vapour spaces are present over the liquids in the calorimeter (but see below) they should be chosen (*e.g.*, they should have widely different vapour pressures) so as to lead to errors at least as large as those which would occur with any pair which it is proposed to study; and (*d*) the heat of mixing should be of the same sign as, and of comparable magnitude to, the heats of mixing which it is proposed to measure. Finally, any such pair should have

[1] McGlashan, "Experimental Thermochemistry," Vol. II, ed. Skinner, Interscience Publ. Inc., New York, to be published in 1961, Chapter 15: "Heats of Mixing."
[2] McGlashan and Morcom, *Trans. Faraday Soc.*, 1961, **57**, 581.
[3] Das, Diaz-Peña, and McGlashan, *Pure Appl. Chem.*, 1961, **2**, 141.

been studied carefully in more than one laboratory and preferably at several different temperatures.

A great majority of the pairs of liquids so far studied mix endothermally with heats of mixing [1] of a few tens or a few hundreds of J $mole^{-1}$. We decided to recommend the pair benzene–carbon tetrachloride for proving a calorimeter which is to be used in that range, and with this in mind, to make some measurements on that pair with the new calorimeter. (The pair carbon tetrachloride–chloroform, which has been used more often than any other for this purpose,[1] has the disadvantages that chloroform is difficult to keep pure, and that the densities differ by only 0·1 g. $ml.^{-1}$.) Benzene and carbon tetrachloride are easily purified and the densities differ by as much as 0·7 g. $ml.^{-1}$. The vapour pressures are nearly identical but this will not matter if future calorimeters are designed, as we hope they always will be, with no vapour spaces, however small, in contact with the liquids. The heat of mixing of benzene with carbon tetrachloride had been studied at 25° in several laboratories [4–10] but even after some selection the results scattered over a range of about 10 J $mole^{-1}$, or about 10% of the heat of mixing of about 110 J $mole^{-1}$ for an equimolar mixture. We were confident that we could improve the accuracy with which the heat of mixing was known by a factor of about ten and expected that the older data would scatter more or less uniformly about ours, though we already suspected that some of them were systematically too low because of incomplete mixing. We have found, however, that the heat of mixing is systematically higher by about 4 J $mole^{-1}$ than we expected. Our measurements are certainly reproducible at worst to about $\pm 0{\cdot}5$ J $mole^{-1}$ and we believe them to be free from systematic errors greater than 0·2 J $mole^{-1}$. We are convinced that the discrepancies arise from incomplete mixing to varying degrees in all the previous calorimeters, and that our measurements are as accurate as we claim. In view of this conclusion, however, the pair benzene–carbon tetrachloride cannot be recommended for proving a new calorimeter until it has "been studied carefully in more than one laboratory." In the meantime we shall be even more sceptical than we were before of calorimeters "proved" with carbon tetrachloride–chloroform or some such pair, which are easy to mix, and then used to study a pair of liquids which are difficult to mix.

Experimental

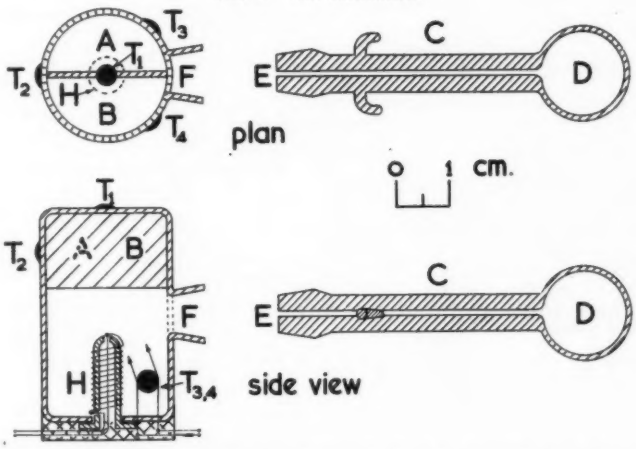
The Calorimeter.—The calorimeter (I) is shown drawn to scale in Fig. 1. It consists of a glass mixing vessel with two compartments A and B in its upper half, and a side-arm, with capillary C and bulb D, which can be attached to the vessel through the ground-glass joint E–F. When the calorimeter is loaded and the side-arm attached, the liquids to be mixed are confined separately, and in the complete absence of vapour spaces, in the compartments A and B by mercury which fills the rest of the vessel and the capillary C (but not the bulb D). Mixing can then be brought about by inverting the vessel. This can be done without allowing the liquids ever to come near the greased joint E–F or the air in the bulb D, by turning the calorimeter several times over and back, through 180° only, in a clockwise direction about an axis through the mixing vessel and perpendicular to the plane of the side view shown in Fig. 1. The capillary C and bulb D provide an air-space in D which, while remaining out of contact with the liquids, ensures that the volume change on mixing causes no appreciable change of pressure [1] in the calorimeter. Four thermistors T (Messrs. Standard Telephones and Cables Ltd., Footscray, Sidcup, Kent: Type M52) connected in parallel were distributed over the outer surface of the vessel and fixed in place with "Araldite" (Messrs. Ciba Ltd., Duxford, Cambs: Type 103 with Hardener 951). At 25° C the combined resistance of the four thermistors was about 100 Ω with a temperature coefficient of about $-3\ \Omega\ °K^{-1}$. A heating coil H with a resistance of about

[4] Cheesman and Whitaker, *Proc. Roy. Soc.*, 1952, *A*, **212**, 406.
[5] Cheesman and Ladner, unpublished measurements; Ladner, Ph.D. Thesis, 1955, University of Reading.
[6] McGlashan and Morcom, unpublished measurements.
[7] Schulze, *Z. phys. Chem.* (*Leipzig*), 1951, **197**, 105.
[8] Brown and Fock, *Austral. J. Chem.*, 1955, **8**, 361.
[9] Brown, Mathieson, and Thynne, *J.*, 1955, 4141.
[10] Hirobe, *J. Fac. Sci. Univ., Tokyo*, 1926, **1**, 155.

40 Ω was made by winding 150 cm. of 38 s.w.g. constantan wire on a glass post. The coil was insulated with " Araldite," and the post was sealed through the bottom of the vessel with " Araldite." [Six of the measurements reported below were made with a calorimeter (II) which differed from (I) only in that the post carrying the heating coil H was inserted into a thin-walled glass pocket which was an integral part of the mixing vessel. Calorimeter (II) was made because " Araldite " appears to be attacked by some of the methylchlorosilanes which we are at present studying.]

The calorimeter was loaded as follows. With the side-arm detached, the mixing vessel was roughly evacuated (to ensure that no air bubbles were trapped by the mercury), completely filled with mercury, and clamped right way up in a trough filled with enough mercury to reach just above the level of the open socket F. A weighed (±0·0002 g.) quantity (0·05—2·5 g.) of one of the liquids to be mixed was then introduced through F into compartment A by means of a hypodermic syringe with a bent needle. A weighed quantity of the other liquid was similarly introduced into compartment B. The side-arm, with the joint E greased, was then immersed in mercury in the trough, the capillary C was filled with mercury, and the side-arm was inserted into the socket F and secured with a spring which passed round the body of the

FIG. 1. *The calorimeter.*



mixing vessel and was hooked on to the two lugs attached to C. The loaded calorimeter was then lifted carefully (so as to prevent premature mixing) from the trough and fitted into a vacuum jacket as shown in Fig. 2.

The vacuum jacket was made in two parts from 75 mm. glass tubing. Each part was joined to an FG75 flat flange glass joint at one end and was closed at the other end. The larger part had a tube K sealed into its closed end, and an opening L. Each part was fitted with a brass collar M made in two halves, seated on cork, and bolted together at N (only one of the two joints N is shown on each collar in Fig. 2). Each collar also carried two projecting pieces P (only one is shown on each collar in Fig. 2) fitted with spring-loaded (Q) bolts R by means of which the (greased) flanges could be held tightly together. The collar M on the larger part was fitted through the shaft S to a stand on which the calorimeter and jacket could be immersed in a thermostat. The stand was fitted with a lever, operated from above the thermostat and acting through an arrangement of gears, by means of which the calorimeter and jacket could be turned over and back through 180° in a clockwise direction about the shaft S. Photographs of a similar stand have been published elsewhere.[3] A length of thick-walled rubber tubing attached to the opening L served both as a flexible connexion to vacuum and as a conduit for the electrical leads allowing the calorimeter to be turned over without detaching it from the vacuum line and without seriously disturbing the electrical leads.

The loaded calorimeter was fitted by means of a rubber sleeve U into the tube K against the rubber seating V. The thermistor and heater leads were connected to the external circuits through the terminal block W. The jacket was bolted together and the whole apparatus

was immersed in a precision thermostat (better than $\pm 0{\cdot}001°$ C), evacuated (to about 10^{-4} mm. Hg), and left overnight to come to thermal equilibrium.

Electrical Circuits.—The heating circuit and clock were as previously described.[2] As previously, a small correction was made for the resistance of the leads of the heating coil. The standard cell and the standard resistance were checked against N.P.L.-certificated Laboratory standards. The stop-watch was checked against B.B.C. time signals.

The thermistor circuit was a Wheatstone's bridge, as shown in Fig. 3, consisting of two arms with fixed resistances of 10Ω and 100Ω, the four thermistors with a combined resistance of about 100Ω, a 0—9999·9Ω five decade resistance box with a resistance of about 1000Ω actually in the circuit, and a galvanometer (Messrs. Tinsley: Type 4500 LS) with a resistance of 33Ω and a maximum current sensitivity of 100 cm. μA^{-1} at a scale-distance of 1 m. The bridge was supplied with current from an accumulator in series with a milliammeter (0—10 mA) and a resistance box X. Before use the accumulator was stabilised by bleeding through a resistance box Y a current adjusted to the same value as would be carried by the bridge. The resistances in the bridge, and the galvanometer, were chosen so as to make the heating effect of the current

FIG. 2. *The vacuum-jacket viewed from above and showing the calorimeter in position.*

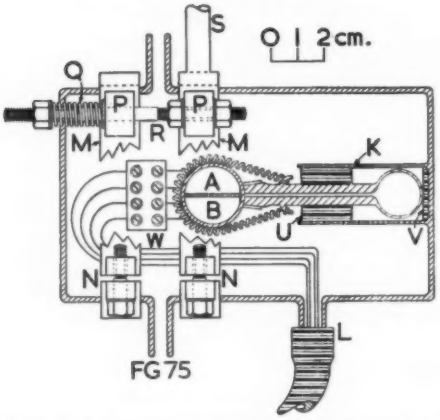
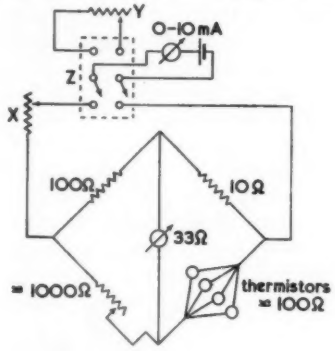


FIG. 3. *The Wheatstone's bridge circuit.*



through the thermistors unimportant compared with the quantities of energy being measured. With the arrangement shown and a bridge current of 6 mA the galvanometer deflexion caused by a change in the temperature of the thermistors was about 700 cm. $°K^{-1}$. The loaded calorimeter had a heat capacity of about 35 J $°K^{-1}$ so that the galvanometer deflexion caused by the introduction of energy into the calorimeter was about 20 cm. J^{-1}. The dissipation of energy by the thermistors had the satisfactorily small value 2×10^{-3} J $min.^{-1}$.

Details of a Typical Experiment.—Galvanometer deflexions Δ plotted against time t are shown for a typical experiment in Fig. 4. In this experiment 0·8686 g. (0·011120 mole) of benzene and 2·0939 g. (0·013612 mole) of carbon tetrachloride were mixed at 25·0° C to give 0·024732 mole of a mixture containing mole fraction $x = 0{\cdot}5504$ of carbon tetrachloride. The complete apparatus was left overnight in the thermostat to come to thermal equilibrium. Just before the experiment the zero reading of the galvanometer was taken. Current (6 mA) was then switched from the bleeding resistance Y to the bridge by throwing the switch Z (see Fig. 3). Galvanometer readings were then taken for 14 min. At 14 min. a current of 0·06220 A was switched to the calorimeter heater and passed for a time $\tau_1 = 19{\cdot}00$ sec. (the clock was started and stopped electrically by the same switch which started and stopped the heating current; details may be found elsewhere [2]). The calorimeter was turned over and back four times beginning a few seconds after 14 min., and twice more at each of the times 15, 16, 17, and 18 min. Galvanometer readings were taken at 0·5 min. intervals from 14 min. until they were again steady (*i.e.*, Δ slowly increasing at a constant rate because of the energy dissipated by the thermistors). This part of the experiment is called the "mixing." At 27 min., when the galvanometer had been steady for several minutes, the calorimeter was

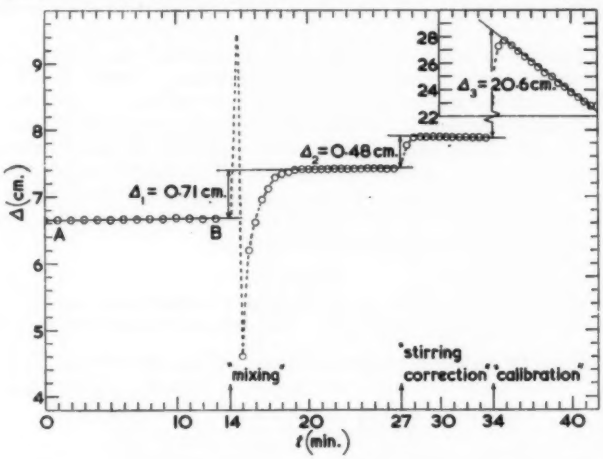
turned over and back twelve times to measure the thermal effect of stirring. This part of the experiment is called the " stirring correction." At 34 min., when the galvanometer had again been steady for several minutes, the current of 0·06220 A was again switched to the calorimeter heater and was passed for a time $\tau_3 = 7{\cdot}89$ sec. Galvanometer readings were again continued until they had been changing linearly with time for several minutes. This part of the experiment is called the " calibration." Finally the galvanometer zero was checked.

The molar heat of mixing $\Delta_m H$ is given by the formula

$$\Delta_m H = i_H^2 R_H\{\tau_1 - (\Delta_1/\Delta_3)\tau_3 + (\Delta_2/\Delta_3)\tau_3\}/(n_1 + n_2) \qquad (1)$$

where i_H (= 0·06220 A) is the current passed through the calorimeter heater, R_H (= 38·64Ω) is the resistance of the heater corrected for the resistance of the leads, τ_1 (= 19·00 sec.) and τ_3 (= 7·89 sec.) are the times for which current was passed through the heater in the " mixing "

FIG. 4. *Galvanometer deflexions Δ plotted against time t for a typical experiment. (The ordinate scale has been reduced by a factor of five for the " calibration " part of the experiment.)*



and " calibration " parts of the experiment respectively, Δ_1 (= +0·71 cm.), Δ_2 (= +0·48 cm.), and Δ_3 (= +20·6 cm.) have the meanings shown in Fig. 4, and $n_1 + n_2$ (= 0·024732 mole) is the total number of moles of the two liquids which were mixed. The numerical values given in parentheses relate to the particular experiment described above. Substituting these numerical values in equation (1) we obtain for that experiment

$$\Delta_m H \text{ (J mole}^{-1}) = 0{\cdot}06220^2 \times 38{\cdot}64\ (19{\cdot}00 - 0{\cdot}27 + 0{\cdot}18)/0{\cdot}024732 = 114{\cdot}3$$

Discussion of Errors.—Reasonable estimates of the upper limits of error in the quantities occurring on the right-hand side of equation (1) are 2×10^{-5} A in i_H, 0·02Ω in R_H, 0·03 sec. in τ_1 and in τ_3, 0·05 cm. in Δ_1 and in Δ_2 (including possible shifts in the galvanometer zero), 0·5 cm. in Δ_3, and 10^{-5} mole in $(n_1 + n_2)$. The overall probable error in $\Delta_m H$ calculated from these individual errors is 0·2$_5$%.

When the (endothermal) heat of mixing is compensated as nearly as possible by the simultaneous introduction of electrical energy [11,12] the error arising from heat losses in the " mixing " part of the experiment is proportional to the difference between the areas above and below the base line (AB in Fig. 4) corresponding to thermostat temperature. In our experiments errors from this source never amounted to more than 0·1$_5$% of the heat of mixing and were usually considerably less. This was so in spite of the rather high value 0·037 min.$^{-1}$ of the coefficient $-$ d ln Δ/dt of Newton's law of cooling for our calorimeter. The value of this

[11] van der Waals, Thesis, 1950, University of Groningen; van der Waals and Hermans, *Rec. Trav. chim.*, 1949, **68**, 181; 1950, **69**, 949; van der Waals, *ibid.*, 1951, **70**, 101.
[12] Adcock and McGlashan, *Proc. Roy. Soc.*, 1954, *A*, **226**, 266.

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coefficient could be reduced by improving the vacuum in the calorimeter jacket and by reducing the losses due to radiation, but such improvements were not thought worth while. The errors arising from heat losses in the " stirring correction " and " calibration " parts of the experiment were negligible.

Incomplete mixing has probably (see below) led to serious errors in some previous measurements of heats of mixing especially when the liquids which were mixed differed markedly in density as is the case for benzene (0·87 g. ml.$^{-1}$) + carbon tetrachloride (1·58 g. ml.$^{-1}$). The reproducibility of the " stirring correction," which we often repeated several times before doing the " calibration " (see Fig. 4), together with the reproducibility of the measurements themselves, made it certain that no errors arose from incomplete mixing in our experiments.

The presence of vapour spaces over the liquids has led to serious errors [1] in many previous measurements of heats of mixing, though in the particular case of benzene (94 mm. Hg at 25° c) + carbon tetrachloride (114 mm. Hg at 25° c) such errors were probably small because of the similarity of the vapour pressures. Since there were no vapour spaces over the liquids in our calorimeter no errors can in any case arise from this source.

Our final estimate of about 0·3% error in $\Delta_m H$ is borne out in the experiments reported below.

Materials.—The benzene was some of that used previously,[13] the purity of which had been established [14] by precise measurements of vapour pressure. Before use it was redistilled through a 27-plate fractionating column and dried over sodium. " AnalaR " carbon tetrachloride was fractionally distilled three times through the same column. A reflux ratio of 10 : 1 was used and the middle fractions only were retained. In the third fractionation the sample was distilled from potassium hydroxide pellets. The product was stored over anhydrous sodium sulphate, small portions being distilled off as required. The density of the carbon tetrachloride was 1·58465 g. ml.$^{-1}$ at 25·0° c; compare 1·58452 which is the mean of the more recent of the values quoted at 25° c by Timmermans.[15]

Results

The results of twenty-six measurements of the heat of mixing of benzene (1) + carbon tetrachloride (2) at 25·0$_0$° c are given in the Table. The first and second columns give the masses

Heats of mixing for mixtures of benzene (1) + *carbon tetrachloride* (2) *at* 25·0° c.

w_1 (g.)	w_2 (g.)	x	ΔH (j)	$\Delta_m H$ (j mole^{-1})	δ (j mole^{-1})
1·2402	0·1272	0·0495	0·405	24·2	+0·4
1·2294	0·2696	0·1002	0·788	45·0	+0·2
1·2119	0·4319	0·1532	1·157	63·2	−0·2
1·1644	0·5723	0·1997	1·427	76·6	−0·6
1·3685	0·9068	0·2517	2·108	90·0	0·0
1·3982	1·1975	0·3031	2·572	100·1	+0·1
1·3911	1·4570	0·3472	2·914	106·8	+0·2
1·1792	1·5409	0·3989	2·810	111·9	−0·1
1·0591 *	1·6653	0·4440	2·801	114·9	+0·2
1·2083	1·9246	0·4471	3·206	114·6	−0·2
1·1716 *	1·9050	0·4522	3·150	115·0	0·0
1·0776	2·0966	0·4970	3·176	115·8	+0·1
1·0487 *	2·0642	0·4999	3·160	115·5	−0·1
0·9729 *	1·9180	0·5003	2·876	115·4	−0·2
0·8686	2·0939	0·5504	2·828	114·3	+0·2
0·7707 *	1·8837	0·5538	2·531	114·5	+0·5
0·8617	2·1076	0·5540	2·808	113·5	−0·4
0·8486 *	2·0776	0·5542	2·775	113·9	0·0
0·7075	2·0439	0·5946	2·480	111·0	0·0
0·5704	2·0634	0·6475	2·173	104·9	0·0
0·5594	2·5320	0·6968	2·280	96·5	−0·6
0·3764	2·2305	0·7505	1·665	86·2	+0·1
0·2825	2·2478	0·8016	1·334	73·2	+0·1
0·2029	2·2763	0·8507	1·021	58·7	+0·3
0·1304	2·1743	0·8944	0·685	43·4	−0·1
0·0592	2·1220	0·9479	0·333	22·9	+0·1

* Measurement made in calorimeter II; all other measurements were made in calorimeter I.

[13] McGlashan and Wingrove, *Trans. Faraday Soc.*, 1956, **52**, 470.
[14] McGlashan and Williamson, *Trans. Faraday Soc.*, 1961, **57**, 588.
[15] Timmermans, " Physico-Chemical Constants of Pure Organic Compounds," Elsevier Publ. Co., Inc., Amsterdam, 1950.

w_1 of benzene and w_2 of carbon tetrachloride and the fourth column gives the measured heat of mixing ΔH. The third column gives the mole fraction x of carbon tetrachloride in the final mixture, and the fifth column gives the heat of mixing $\Delta_m H$ per mole of final mixture. The last column will be discussed below.

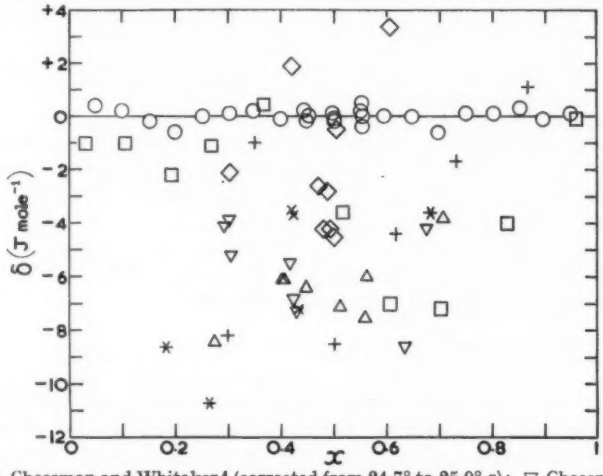
Discussion

Our measurements have been fitted by the equation

$$\Delta_m H \text{ (J mole}^{-1}) = x(1-x)\{462{\cdot}6 + 16(1-2x) + 25(1-2x)^2 + 10(1-2x)^3\} \quad (2)$$

Values of the excess δ of the measured value of $\Delta_m H$ over that calculated from equation (2) are shown in the sixth column of the Table. The root mean square value $\langle\delta^2\rangle^{\frac{1}{2}}$ of δ is $0{\cdot}2_6$ J mole^{-1}, in good agreement with the value calculated above for the probable experimental error. For only five of the twenty-six measurements is $|\delta|$ greater than 0·3 J mole^{-1}.

Fig. 5. *The excess δ of the molar heat of mixing $\Delta_m H$ over the value calculated according to equation (2), plotted against the mole fraction x of carbon tetrachloride for benzene + carbon tetrachloride at 25·0° c.*



○ This work; △ Cheesman and Whitaker [4] (corrected from 24·7° to 25·0° c); ▽ Cheesman and Ladner [5] (corrected from 24·4° to 25·0° c); ◇ McGlashan and Morcom [6] (corrected from 24·8° to 25·0° c); □ Schulze; [7] × Brown and Fock; [8] * Brown, Mathieson, and Thynne; [9] + Hirobe.[10]

A comparison of our results with those of previous workers is shown in Fig. 5 where δ is plotted against the mole fraction x of carbon tetrachloride. Three of the previous sets of measurements (see the legend to Fig. 5) were made at temperatures a few tenths of a degree below 25° c. They have been corrected to 25·0° c with amply sufficient accuracy by assuming [4,7,16] that $d\Delta_m H/dT = 5{\cdot}8x(1-x)$ J °K^{-1} mole^{-1}.

The scatter of our measurements is much less than that of any of the previous sets. Much more striking, however, is the fact that our values of $\Delta_m H$ are higher, in some cases by as much as 8% or more, than nearly all previous values, and higher by about 4 J mole^{-1} than we had expected after consideration of the previous values. We are convinced that the discrepancies are due mainly to incomplete mixing in previous calorimeters. Canning and Cheesman,[17] using the same calorimeter and technique as Cheesman and Whitaker,[4] found that benzene (0·87 g. ml.$^{-1}$) + bromobenzene (1·49 g. ml.$^{-1}$) did not mix completely. If this was so it is difficult to believe that benzene (0·87 g. ml.$^{-1}$) + carbon tetrachloride (1·58 g. ml.$^{-1}$) were completely mixed in Cheesman and Whitaker's experiments. Cheesman and Ladner mentioned the possibility that incomplete mixing had led to hidden

[16] Boissonas and Cruchaud, *Helv. Chim. Acta*, 1944, **27**, 994.
[17] Canning and Cheesman, *J.*, 1955, 1230.

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errors in their published measurements [18] on pairs of liquids with density differences less than 0·02 g. ml.$^{-1}$. If this was so it is difficult to believe that there were not much bigger errors from this source in their unpublished measurements [5] on benzene + carbon tetrachloride. McGlashan and Morcom's measurements,[6] made in a calorimeter [12] which we now regard as superseded, are in better agreement with our present measurements in spite of a scatter about ten times as great. Schulze's measurements [7] are in fair agreement with ours for mixtures rich in benzene.

We hope that benzene + carbon tetrachloride will soon be studied somewhere else in a calorimeter capable of a precision similar to or better than ours and in which it is certain that mixing is complete.

[*Added in proof*: We have now made five further measurements with a different sample of benzene (supplied by the National Chemical Laboratory with a certified purity of 99·990 ± 0·002 moles %), and a different sample of carbon tetrachloride (kindly given to us by Mr. L. A. K. Staveley; we find 1·58462 g. ml.$^{-1}$ for its density at 25·0°). The results, namely:

x	0·3007	0·4002	0·4983	0·5993	0·6999
δ(J mole^{-1})	+0·1	+0·6	+0·7	+0·5	+0·4

are systematically higher than those given in the Table but by an amount which is only just outside our experimental error.]

We are grateful to Dr. S. K. Das and to Dr. M. Diaz-Peña for their help in the earlier stages of the design of the calorimeter. This work has been carried out partly under the terms of a contract made by the Department of Scientific and Industrial Research for its National Engineering Laboratory.

Department of Chemistry,
The University, Reading. [*Received, February 22nd*, 1961.]

[18] Cheesman and Ladner, *Proc. Roy. Soc.*, 1955, *A*, **229**, 387.

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667. *Optical Studies of the Soret Effect. Part I. A Modified Optical Beam-displacement Method and its Application to Aqueous Silver Nitrate Solutions.*

By H. J. V. Tyrrell, J. G. Firth, and M. Kennedy.

An optical method of studying the Soret effect is described; it involves a modified Tanner cell. Results for m- and 2m-silver nitrate at a mean temperature of 25°, obtained for different applied temperature gradients, have been used in calculating Soret coefficients by different methods. The results obtained from a given set of data were not quite identical, principally because of theoretical difficulties. A satisfactory method of calculation is described which gives values of this parameter which are independent of cell height, of the position of the exploring beam in the cell, and of temperature gradient, and the advantages of using a cell with a small separation between the hot and the cold plate with this beam-displacement method are demonstrated. Soret coefficients for solutions between 0·1m and 8m at several mean temperatures have been obtained, and entropies of transfer for silver nitrate have been calculated as a function of solution concentration at 25°.

The Soret phenomenon, that is, the partial separation of the components (demixing) of a binary solution under the influence of a temperature gradient, has recently attracted increasing attention, both experimentally and from the theoretical point of view.[1,2] The

[1] Bierlein, *J. Chem. Phys.*, 1955, **23**, 10.
[2] Agar, *Trans. Faraday Soc.*, 1960, **56**, 776.

primary aim of experimental work in this field is to deduce the Soret coefficient (σ), which may be conveniently defined [3] as

$$\sigma = -\frac{1}{m}\left(\frac{\text{grad } m}{\text{grad } T}\right)_{\text{stat.}}, \quad (1)$$

from the experimental results. In equation (1) the suffix " stat." denotes that the concentration gradient is measured in the time-invariant steady state in which the flow of matter caused by the temperature gradient is balanced by the flow in the reverse direction under the influence of the concentration gradient. Usually the temperature gradient is applied to a vertical column of the liquid solution in such a way as to eliminate as far as possible the effects of convection, and the concentration changes are followed by measuring the change of some physical property with time. For dilute electrolyte solutions, measurements of the ratio of the resistances of the upper and the lower half of the Soret cell have been used successfully; [4-7] for somewhat more concentrated solutions it has been suggested [7,8] that an adaptation of Harned and French's conductimetric method [9] of studying the isothermal diffusion of dilute electrolytes would be satisfactory. For even more concentrated solutions of electrolytes, and for non-electrolyte mixtures, optical methods have been quite widely used. These fall into two main classes:

(i) Interference (" integral fringe ") methods. Longsworth [10] used a twin Soret cell in conjunction with a Rayleigh interferometer for a detailed study of several concentrated aqueous electrolytes. He showed that an integrated diffusion equation due to Bierlein [1] gave a good but not perfect representation of the rate at which the steady state was attained. In an attempt to minimize first-order variations in σ with temperature, fringe patterns formed at planes disposed symmetrically about the cell centre were used. A second method in which refractive-index differences at two planes placed symmetrically above and below the cell centre were measured directly in a conventional Soret cell [11] gave results for fairly concentrated potassium chloride solutions which agreed well with those found by Longsworth.[12]

(ii) Beam displacement methods. In these the refractive-index gradient in the unequally heated liquid column is measured. Tanner [13,14] measured this gradient as a function of cell height over almost the whole height of the cell. Other workers have usually limited their observations to measuring either the average refractive-index gradient over a large part of the cell height [15,16] or that over a limited region explored by a narrow horizontal light beam entering the cell at a known level.[17]

In diffusion work, interference-fringe methods are preferred because of the accuracy with which fractional fringe shifts can be measured. However, in studies of the Soret effect other difficulties tend to reduce this advantage. For example, Longsworth [10] was unable to design a twin cell with fully satisfactory thermal properties. Also the cell must be fairly tall, and, for adequate sensitivity, quite a large temperature interval must be used. Furthermore, the optical equipment used must be of high quality. Beam-displacement methods, on the other hand, are less demanding in the last respect and possess one great advantage which has hitherto been almost entirely ignored. Since the

[3] Cf., *e.g.*, Tyrrell, *Trans. Faraday Soc.*, 1960, **56**, 770.
[4] Agar, " The Structure of Electrolytic Solutions," ed. Hamer, Wiley, New York, 1959, p. 213.
[5] Agar and Turner, *Proc. Roy. Soc.*, 1960, *A*, **255**, 307.
[6] Snowden and Turner, *Trans. Faraday Soc.*, 1960, **56**, 1409.
[7] Snowden and Turner, *Trans. Faraday Soc.*, 1960, **56**, 1812.
[8] Agar and Turner, *J. Phys. Chem.*, 1960, **64**, 1000.
[9] Harned and French, *Ann. New York Acad. Sci.*, 1945, **44**, 267.
[10] Longsworth, *J. Phys. Chem.*, 1957, **61**, 1557.
[11] Chanu and Lenoble, *Compt. rend.*, 1955, **260**, 949; *J. Chim. phys.*, 1956, **53**, 309.
[12] Tyrrell, " Diffusion and Heat Flow in Liquids," Butterworths, London, 1961.
[13] Tanner, *Trans. Faraday Soc.*, 1927, **23**, 75.
[14] Tanner, *Trans. Faraday Soc.*, 1953, **49**, 611.
[15] Korsching, *Z. Naturforsch.*, 1955, **10a**, 242.
[16] Bierlein, Finch, and Bowers, *J. Chim. phys.*, 1957, **54**, 872.
[17] Thomaes, *Physica*, 1951, **17**, 885.

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gradient of refractive index is measured, it is the temperature *gradient* which determines the sensitivity, not the temperature interval between the cell plates as in the integral-fringe methods described. Hence, if the distance between the cell plates is reduced, the temperature interval between them can be reduced in the same proportion without loss of sensitivity. It has been reported [16] that the value of σ calculated from beam-displacement measurements with the available equations depends on the temperature interval used and it would seem to be advantageous to reduce it as far as possible. Further, the time required for a given experiment is proportional to the square of the cell height, while the greater the area : height ratio the smaller is the likelihood that convective remixing will affect the results. The only experimental work on these lines reported hitherto is that of Whitaker and Pigford [18] who used a brass cell with a plate distance of only 2 mm. However they were concerned mainly with a broad study of non-electrolyte pairs and it is difficult to judge the real potentialities of the method from their results.

Some years ago a paper from this laboratory [19] described the results of some Soret coefficient measurements obtained on the second apparatus designed by Tanner.[14] On this basis, modified cells have been designed and their performances evaluated by using them to study the Soret coefficients of silver nitrate solutions of different concentrations over a range of mean temperatures with different temperature gradients. These solutions were chosen because the original cell was not well adapted to work with non-aqueous solutions, while silver nitrate in water has a relatively large Soret coefficient. Also, some diffusion measurements are available on this system, and this permits Soret coefficients to be calculated from the experimental data on one type of modified cell by several methods. Since isopiestic activity coefficients are available at 25° for silver nitrate solutions from 0·1 molal upwards,[20] it has been possible to obtain the sum of the ionic entropies of transfer ($S^*_+ + S^*_-$) from the calculated Soret coefficients.

Experimental

The optical system is shown in Fig. 1. A horizontal adjustable slit A is illuminated through condenser lens B by a high-pressure mercury arc C (Mazda type ME-D). Behind the slit A are placed a Compur shutter and a Wratten green filter (No. 77) (D) which transmits light of λ 5461 Å. Light from this slit is rendered parallel by the lens E (f 12 cm.) and then passes through a horizontal double slit F (cf. Thomaes [17]) whose vertical position relative to the optic axis could be adjusted accurately. The Soret cell G was placed immediately after the double slit, and the light issuing from it was focused by a Zeiss achromat H of 50 cm. focal length on to a vertical graticule scale I placed in the image plane. The diffraction image of A formed in this plane had a strong central band which was split into a sharp interference pattern. This was photographed against the scale lines of the graticule by a low-power microscope objective attached to a plate camera, arranged so that a number of successive exposures could be made on the same plate. Ilford Selochrome plates were used, with a high-contrast developer. Under the conditions of exposure and development adopted, the photographic image consisted of three dark bands on a transparent background, the marks on the graticule showing as clear lines in the darkened areas. Displacements of the fringe pattern were measured by using a travelling microscope (5 × magnification), with any convenient line in the graticule as a reference line. After a little experience, the position of the fringe pattern relative to the graticule could be determined with a reproducibility of 10 microns. During the course of an experiment no change in the width of the fringe pattern could be detected; it was simply displaced as a whole.

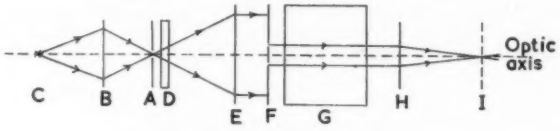
The original cell used, shown in Fig. 2a, was that designed and described by Tanner.[14] In the later work on m-silver nitrate a redesigned glass cell chamber was used with the same silver discs. The plane glass windows in the new chamber were small and circular, and the inner surfaces were arranged to be 7·63 cm. apart, that is, they formed tangents to the circular silver plates (Fig. 2b). They were sealed in position by small O ring seals, and the cell was

[18] Whitaker and Pigford, *Ind. Eng. Chem.*, 1958, **50**, 1026.
[19] Tyrrell, Chapman, and Wilson, *J.*, 1957, 2135.
[20] Robinson and Stokes, "Electrolyte Solutions," Butterworths, London, 1954, Appendix 8–10.

therefore suitable for use with non-aqueous solutions.[21] A somewhat more uniform temperature gradient was obtained in a rectangular cell of a radically different design, but other factors prevented its extensive use. On the whole, the cell of circular section has many advantages over other forms.

The temperatures of the upper and the lower plate were controlled by circulating through them water from thermostat baths of large capacity, and were measured by multi-junction thermocouples (copper–constantan, 5 junction) placed in the sockets shown in Fig. 2. At the

FIG. 1. *Optical system (vertical section).*

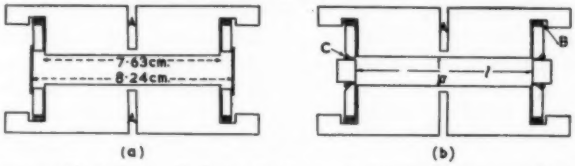


beginning of an experiment, the two plates were held at the same temperature until thermal equilibrium was reached. Then, by operating a series of quick-release valves (Saunders) in the pumping system, water at the higher temperature was passed through the upper plate, and that at the lower temperature through the lower plate. To minimise heat losses from

FIG. 2. *Experimental Soret effect cells.*

(a) *Unmodified Tanner cell.* (b) *Modified cell with small tangential windows.*

The upper half of the cell is separated from the lower half by three Tufnol (or Nylon) spacing rods outside the circular glass wall of the cell. These are not shown.



A,A *Thermocouple pockets.* B *Large* ○ *rings.* C *Small* ○ *rings round the windows.*

the cell, the whole of the optical layout was enclosed in an air-thermostat maintained at the mean temperature of the experiment with an accuracy of $\pm 0{\cdot}2°$.

Before an experiment, the lower plate of the cell was set up at the correct height and levelled to 30 seconds of arc by means of a precision clinometer. The body of the cell was then assembled, and the top plate dropped into position and compressed lightly against the three Tufnol (or Nylon) spacing rods. The cell was filled with de-aerated solution, and the pressure on the top plate adjusted until the distance between the top and the bottom surface was within 10 microns of the desired value at a number of points on the periphery of the cell. These measurements, of course, also gave an accurate measure of the cell height. By this means, both plane-bounding surfaces in the cell were made horizontal and parallel to the highest degree of accuracy available to us. It was not possible to ensure that the cell walls were also vertical to the same degree of precision. Finally, the double slit was adjusted to a known position relative to the base of the cell, also with an accuracy of 10 microns.

Bierlein, Finch, and Bowers [16] have described a similar optical arrangement in which the position of the interference pattern in the beam passing through the cell is compared with that of a similar undeflected beam which has passed through air. In this way small shifts due to changes in the mechanical or optical parts of the apparatus were said to be eliminated. We have tried incorporating such a device in the present apparatus, but found that the only shifts observed in the reference pattern were due to changes in the mercury arc during the warming-up stage. By ensuring that the lamp had been running for some time before observations were begun, the observed shifts in the reference beam in the present apparatus were found to be negligible and this refinement was unnecessary in our experimental conditions.

Solutions were made up by weight from " AnalaR " silver nitrate and distilled water (which

[21] Tyrrell and Faine, unpublished work.

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had been passed through a mixed-bed ion exchange column). Refractive indices were measured on a Bellingham and Stanley refractometer of an improved Pulfrich pattern. The refractive-index increment with concentration was obtained from measurements on a series of solutions whose composition increased successively by 0·5 molality unit. Between 0 and 1 molal this quantity remained constant, and was used in interpreting Soret effect measurements on solutions up to 0·5m. At concentrations above 1m, it slowly decreased, and, from this concentration upwards, the mean of the increments measured between $(x - 0{\cdot}5)$ and x, x, and $(x + 0{\cdot}5)$, was assumed to be the value characteristic of an x-molal solution. The change with temperature was found from the observed constant deflection of a beam entering the 10 mm. cell at $\xi_1 = 0{\cdot}5$ in the time interval between the establishment of the temperature gradient and the onset of demixing in this plane. This was not noticeable when $t < 0{\cdot}1\theta$, or less than 10 minutes from the time at which the temperature gradient was first applied.

Results and Discussion

Temperature Distribution in the Soret Cells.—The temperature coefficient of refractive index (dn/dT) for water is known accurately,[22] and, when the cell is filled with water, the temperature gradient at any given plane can be deduced from the deflection of a light beam passing through the cell at that plane. Strictly, because of the finite width of the beam and the bending of the beam within the cell, the average temperature gradient over a small vertical height in the cell is found by using the equation

$$dT/d\xi = Z_\xi(a/lf)(dn/dT)^{-1}, \qquad (2)$$

where ξ is the " reduced height " in the cell defined as the ratio z/a (z is the height of the plane explored above the bottom of the cell which has a total height a); the effective optical path length within the cell is l, and the focal length of the image-forming lens H is f; and Z_ξ is the observed deflection for light passing through the plane identified as ξ. By using a series of identical double slits arranged one above the other and suitably masked, it was possible to explore the temperature gradient at a number of planes in the cell in a relatively short time.

Some early experiments were carried out with the cell shown in Fig. 2a. The temperature gradient within this cell did not vary by more than 1—2% over the region $\xi = 0{\cdot}2$—$0{\cdot}8$, but the average value calculated from eqn. (2) by using the geometrical distance between the inner surfaces of the windows as a measure of l was considerably less than that calculated from the thermocouple readings. By means of the latter, the effective optical path length in the cell could be calculated and was found to be very close to the diameter (7·63 cm.) of the silver discs. This observation is important in assessing some of the earlier work done with this type of cell.[14,19] This uncertainty was absent in the modified cell shown in Fig. 2b, but the temperature gradient in it was rather less uniform and not quite symmetrical about the median plane of the cell (Fig. 3). A similar cell in which the distance (a) between the discs was reduced to 2 mm. was also examined. With a total temperature interval between the thermocouples of 1·96°, the temperature gradient in the cell was substantially constant at all planes and ~1% less than that calculated from the thermocouple readings and the cell height. This corresponds to a temperature difference of 0·01° between the thermocouples and the disc faces, which would not be surprising.

Measurement of Soret Coefficients.—The total refractive-index gradient ($dn/d\xi$) in the cell, when this is filled with a solution, is the sum of two terms, one arising from the concentration gradient and the other from the temperature gradient, and can be expressed as

$$\frac{dn}{d\xi} = \frac{dN}{d\xi}\left(\frac{\partial n}{\partial N}\right)_T + \tau\left(\frac{\partial n}{\partial T}\right)_N$$

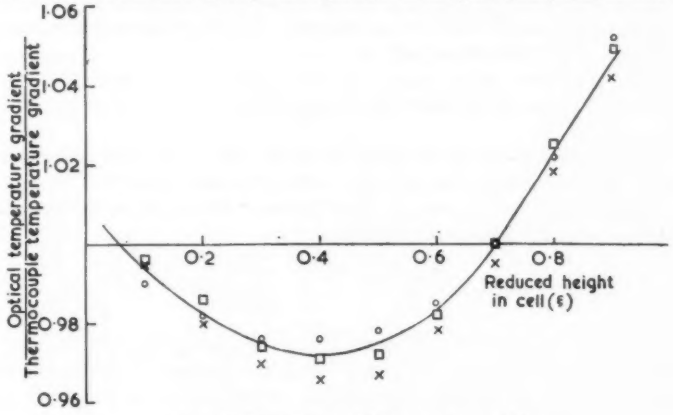
[22] Tilton and Taylor, *J. Res. Nat. Bur. Stand.*, 1938, **20**, 419.

where N is the mole fraction, and τ the temperature interval across the cell, the temperature gradient being assumed to be constant at all points in the cell. As shown in the previous section this constancy does not always exactly hold. The gradient of concentration in the cell can only be obtained in terms of the Soret coefficient from the diffusion equation (J_i = flow of component i per unit area per unit time, ρ is the density of the solution),

$$J_i = -\frac{D\rho}{a}\left(\frac{dN_i}{d\xi} + \sigma\tau N_i(1 - N_i)\right),$$

integrated subject to the boundary conditions appropriate to the cell. A full solution of this problem has not been achieved, but several approximate forms have been

FIG. 3. *Vertical variation of temperature gradient in modified, water-filled, Tanner cell.*



× $\tau = 9{\cdot}96°$. ○ $\tau = 6{\cdot}98°$. □ $\tau = 5{\cdot}00°$.

proposed [1,2,23] of varying degrees of complexity, all of which assume that the temperature gradient, the diffusion coefficient D, and the Soret coefficient are constant throughout the cell. A useful approximate form which can be derived from either Bierlein's [1] or Agar's [2] treatment is (cf. ref. 12, p. 202):

$$Z_{\xi,t} = \frac{lf}{a}\left[K_2 - \sigma\tau K_1\left\{1 - \frac{2}{\pi}\sum_{j=1}^{\infty}[1 - (-1)^j]\frac{1}{j}\sin j\pi\xi \exp(-j^2t/\theta)\right\}\right]. \quad (3)$$

$Z_{\xi,t}$ is the observed deflection at time t of a beam passing through the cell in the plane ξ; $K_1 = N_1^0(1 - N_1^0)(\partial n/\partial N_1)_T$; $K_2 = \tau(\partial n/\partial T)_N$; and $\theta = a^2/\pi^2 D$. The series converges most rapidly when $\xi = \frac{1}{3}, \frac{2}{3}$, and at these planes equation (3) can be replaced by

$$Z_{\xi,t} - Z_{\xi,\infty} = \frac{4lf}{\pi a}\sigma\tau K_1 \sin\pi\xi \exp(-t/\theta) \quad (4)$$

after a very short time. In this, $Z_{\xi,\infty}$ is the steady-state deflection, since, from (3), when $t = \infty$, we have

$$Z_{\xi,\infty} = \frac{lf}{a}(K_2 - \sigma\tau K_1). \quad (5)$$

Elsewhere in the cell the higher terms in the sum of equation (3) remain important for longer.

If the diffusion constant, and hence θ, is unknown, a plot of $\ln(Z_{\xi,t} - Z_{\xi,\infty})$ against t

[23] de Groot, " L'Effet Soret," North Holland, Amsterdam, 1947.

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should be linear with a slope of $(-1/\theta)$, except when t is small, and an intercept at $t = 0$ from which σ can be calculated (method 1). Alternatively, if an independent value of D is available, $Z_{\xi,t}$ should be a linear function of $\exp(-t/\theta)$, the slope being proportional to σ (method 2). Extrapolation of this linear plot to $t = \infty$ yields a value of $Z_{\xi,\infty}$ derived from measurements of $Z_{\xi,t}$ in the earlier stages of the experiment. Both this extrapolated value and the directly observed one can be used in equation (5) to calculate σ (methods 3 and 4 respectively). They should, of course, be the same, but there are some experimental difficulties in the way of a direct observation of $Z_{\xi,\infty}$ and Bierlein, Finch, and Bowers [16] in their work on n-heptane–benzene mixtures preferred to use the extrapolated value which they found to differ significantly from the directly measured one. In methods 1 and 2, direct determination of the Soret coefficient from the plot involves the term $(\sin \pi\xi)$. The entrance plane at which the centre of the beam impinges on the cell can be determined quite accurately, but, through the cell, the beam follows a parabolic path and emerges at a plane lower than that at which it has entered. If the entrance plane is at ξ_1 and the exit plane at ξ_2, it can be shown that [24]

$$\xi_1 - \xi_2 = \frac{l}{2naf} \cdot Z_{\xi,t}, \qquad (6)$$

where n is the refractive index of the solution in the cell. The observed deflection in the image plane is proportional to the average refractive-index gradient over the path explored; provided that ξ_1 and ξ_2 are not very different this is given by equation (3) with ξ replaced by $(\xi_1 + \xi_2)/2$. From equation (6),

$$\xi \equiv \frac{\xi_1 + \xi_2}{2} = \xi_1 - \frac{l}{4naf} \cdot Z_{\xi,t},$$

$Z_{\xi,t}$ is a function of time and $(\sin \pi\xi)$ must also vary during the experiment. However, a large proportion of the observed deflection in the image plane is due to the temperature gradient, and this remains constant during the establishment of the Soret equilibrium. For the purpose of calculating σ by methods (1) or (2) it is reasonable to take the value of $Z_{\xi,t}$ to be used in equation (6) as the mean between that due to the temperature effect alone and that observed when the steady-state equilibrium has been reached. Strictly, the plots used in methods (1) and (2) should not be exactly linear because of this time-variation of $Z_{\xi,t}$, but the effect is too small to be seen; the choice of ξ to be inserted in equation (3) does, however, make a small difference to the calculated Soret coefficients.

Experiments on the rate of attainment of the steady state have been carried out on m- and 2m-solutions. At $\xi = \frac{1}{3}$, $\xi = \frac{2}{3}$, the plots of $\log(Z_{\xi,t} - Z_{\xi,\infty})$ against time were accurately linear for $t > 0{\cdot}1\theta$. Fig. 4 shows a plot of $Z_{\xi,t}$ against $\exp(-t/\theta)$ for a m-solution, θ having been calculated from Longsworth's value [25] of the diffusion coefficient at 25°. The observed value of $Z_{\xi,\infty}$ agreed closely with the extrapolated value derived from a least-squares analysis of the data from an earlier stage of the experiment. Similar results were obtained for 2m-solutions except that the extrapolated value of $Z_{\xi,\infty}$ was consistently 2—4% below the measured value. Parasitic remixing processes in the cell would have produced the opposite effect. However, it was found that small changes in the value chosen for θ changed the slope and intercept of the exponential plot significantly without noticeably affecting the linearity. The only value of the diffusion coefficient available to us was derived from some diaphragm-cell measurements,[26] a method which is not very suitable for use with this solution, and it is possible that it was slightly in error.

Table 1 shows some isothermal diffusion measurements derived from the slopes of

[24] Tyrrell, *Trans. Faraday Soc.*, 1956, **52**, 940.
[25] Longsworth, "The Structure of Electrolytic Solutions," ed. Hamer, Wiley, New York, 1959, p. 194.
[26] Firth, unpublished work.

the logarithmic plots which may be compared with Longsworth's value of $1{\cdot}276 \times 10^{-5}$ cm.^{2} sec.$^{-1}$.

TABLE 1. *Diffusion coefficients for* m-*silver nitrate solutions from Soret effect measurements.* $T_m = 25°$ *at centre of cell* ($\xi = 0{\cdot}5$). *Cell:* 1 *cm. high, thick windows.*

Plane of entry, ξ_1	0·321	0·655	0·321	0·655	0·321	0·655
Temperature gradient (° c cm.$^{-1}$)	10·01	10·00	7·01	7·00	5·00	5·00
Calc. diffusion coeff. (10^{-5} cm.^{2} sec.$^{-1}$)	1·208	1·246	1·268	1·279	(1·335)	1·27

When the temperature gradient was high, the measured diffusion coefficient was below the true value, and it increased towards the correct one as the temperature gradient was reduced. The value in parentheses is exceptionally high, and may indicate that there was some convective remixing in the cell during this experiment, though there is little evidence in the Soret coefficients calculated from these measurements that the experiment was abnormal (cf. Table 2).

An investigation of the effect of the size of the temperature interval upon the magnitude of the calculated Soret coefficient derived from data of the kind available here may be vitiated by an incorrect choice of the mean temperature in the cell. The mean refractive-

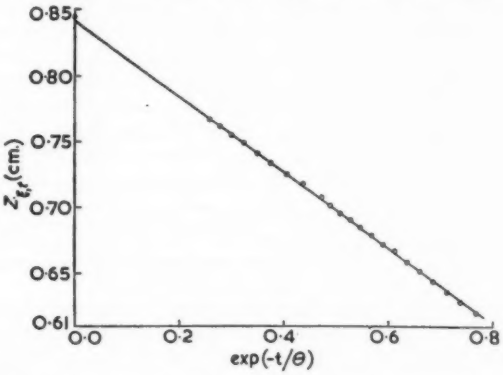

FIG. 4. *The rate of attainment of Soret equilibrium in aqueous* m-*silver nitrate* ($\tau = 10{\cdot}00°$; $\xi_1 = 0{\cdot}655$; 25° *at* $\xi = 0{\cdot}5$).

Plot of $Z_{\xi,t}$ *against* $\exp(-t/\theta)$ *with* $D = 1{\cdot}276 \times 10^{-5}$ cm.^{2} sec.$^{-1}$ (Longsworth, ref. 24).

index gradient over a limited vertical height in the cell has usually been measured in this work at $\xi \sim \frac{1}{3}$ or $\frac{2}{3}$, these values being chosen to make the higher terms in the sum appearing in equation (3) diminish to insignificance as rapidly as possible. At first sight, it might be assumed that, since the local refractive-index gradient is being measured, the calculated Soret coefficient values must refer to the region explored. If this were the case, it would be correct to keep the mean temperature at this plane the same from one experiment to another. If this is done for investigations at $\xi = \frac{1}{3}$, the temperature at the centre of the cell will be higher than that at the plane explored, and will fall as the temperature interval across the cell decreases. When the region round $\xi = \frac{2}{3}$ is studied, the temperature at the cell centre will be less and will rise as the temperature interval is decreased. However, this simple view can hardly be correct since the cell is bounded at $\xi = 0$, $\xi = 1$, and the diffusion processes at any plane cannot be independent of those proceeding elsewhere in the cell. A solution of the diffusion equation for the case of a variable Soret coefficient has not been satisfactorily achieved though an attempt has been made by one of us [27] assuming a linear variation of σ with temperature. It is difficult to estimate the effect of some of the approximations used in this treatment on the final result but we have concluded that, no matter where the refractive-index gradient is measured in the cell, the Soret coefficient calculated from the data refers to that at the cell centre. If this is so, the temperature at $\xi = 0{\cdot}5$ should be kept constant when changing

[27] Kennedy, Ph.D. Thesis, Sheffield, 1960.

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the temperature interval. Soret coefficients, calculated by methods (1) and (3) only, from experiments on 2m-solutions in which the exploring beam entered the cell at $\xi = \frac{1}{3}$, the temperature in this plane being unchanged, showed a marked decrease with the size of the temperature interval, especially when method (1) was used. A linear extrapolation to zero temperature gradient gave a value of about $7{\cdot}3 \times 10^{-3}$ deg.$^{-1}$ but the uncertainty in this figure is quite large. A more extensive study with m-solutions, for which a reliable value of the diffusion coefficient is available, was then carried out with modified Tanner cells having $a = 10$ mm. and $a = 2$ mm. Results on the first cell are given in Tables 1 and 2. Soret coefficients calculated by the four methods described are shown in Table 2

TABLE 2. *Soret coefficients for aqueous* m*-silver nitrate calculated from results obtained from a modified Tanner cell* ($a = 10$ mm.).

Plane of entry, ξ_1	Temp. gradient (° c cm.$^{-1}$)	Approx. ξ at which $T = 25°$	Calc. Soret coefficients (deg.$^{-1}$ × 10^3) Method 1	Method 2	Method 3	Method 4
0·321	10·02	$\frac{1}{3}$	4·69 (4·28)	4·68 (4·29)	4·67 (4·42)	4·65 (4·42)
0·655	10·27	$\frac{2}{3}$	3·87	3·90	4·18	4·20
0·321	7·00	$\frac{1}{3}$	4·51 (4·27)	4·50 (4·28)	4·36 (4·35)	4·38 (4·37)
0·655	7·00	$\frac{2}{3}$	4·03	4·07	4·34	4·36
0·321	4·49	$\frac{1}{3}$	4·49 (4·31)	4·55 (4·33)	4·49 (4·44)	4·36 (4·33)
0·655	5·01	$\frac{2}{3}$	4·14	4·11	4·40	4·30
0·321	10·01	$\frac{1}{2}$	4·54 (4·33)	4·49 (4·31)	4·42 (4·39)	4·30 (4·32)
0·655	10·00	$\frac{1}{2}$	4·13	4·13	4·37	4·34
0·321	7·01	$\frac{1}{2}$	4·42 (4·28)	4·43 (4·31)	4·45 (4·39)	4·45 (4·41)
0·655	7·00	$\frac{1}{2}$	4·14	4·16	4·34	4·37
0·321	5·00	$\frac{1}{2}$	4·44 (4·32)	4·49 (4·36)	4·37 (4·37)	4·48 (4·42)
0·655	5·00	$\frac{1}{2}$	4·21	4·23	4·37	4·37

Notes. Method 1: From intercept of log $(Z_{\xi,\infty} - Z_{\xi,t})$ against time. Method 2: From slope of $Z_{\xi,t}$ against exp $(-t/\theta)$ with independent value of diffusion coefficient. Method 3: From measured steady-state deflection. Method 4: From steady-state deflection obtained by extrapolation from plot used for method 2.

Figures in parentheses represent the mean value of the pair.

for observations taken at $\xi = \frac{1}{3}$, $\xi = \frac{2}{3}$, with three different temperature gradients. In half the experiments, the temperature at the plane explored was held at 25°; in the other half, the temperature at the cell centre was kept at this value. For the first set the Soret coefficients calculated by methods (1) and (2) are considerably larger from data obtained at $\xi_1 = 0{\cdot}321$ than at $\xi_1 = 0{\cdot}655$, the difference falling slightly with the temperature gradient. Differences of this kind are too large to be explicable in terms of the uncertainty in ξ due to the bending of the beam in its passage through the cell as discussed earlier. The mean of each pair of values, however, varies very little with the temperature gradient. The differences between the pairs of coefficients calculated by methods (3) and (4) are not so marked; indeed, except when the temperature gradient had its largest value, they were scarcely significant. Once again, the change in the mean of each pair with temperature gradient was small, but the mean value for all observations, calculated by these methods, was distinctly larger than the similar figure calculated by methods (1) and (2); if appreciable convective remixing had occurred during the experiments, it should have been smaller. The same general pattern emerges from a study of the second group for which the temperature at $\xi = \frac{1}{2}$ was kept constant, though the differences between pairs of values, calculated by methods (1) and (2), from data at $\xi_1 = 0{\cdot}321$, and at $\xi_2 = 0{\cdot}655$ are somewhat less than before. For methods (3) and (4), the differences are even smaller. These results are consistent with the view that the calculated value of the Soret coefficient is characteristic of that at the centre of the cell and that, even on this assumption, equation (3) is not entirely adequate to describe the variation in the refractive-index gradient with time (cf. Longsworth [10]).

The mean values in the second set display an independence of the temperature gradient similar to that found for the first. Furthermore, if all the results are examined, it will

be seen that methods (1) and (2) on the one hand, and methods (3) and (4) on the other, nearly always give calculated coefficients in close agreement for any given set of experimental results. This shows that these experimental results are consistent with Longsworth's measurements on the isothermal diffusion coefficient of m-silver nitrate, and it thus reinforces the conclusion drawn from the data in Table 1.

Because of experimental difficulties, the planes explored in the upper and the lower section of the cell were not quite symmetrical about the centre. Since the calculated coefficients probably refer to the value at the cell centre rather than to that characteristic of the plane explored, this small defect should be less important for the second set of results in Table 2, and the following discussion is confined to these. The mean of all the values shown in parentheses derived by methods (1) and (2) is $4{\cdot}31 \times 10^{-3}$ deg.$^{-1}$, the standard deviation of this mean being $0{\cdot}011 \times 10^{-3}$ deg.$^{-1}$. For methods (3) and (4) the corresponding quantities, in the same units, are 4·38 and 0·014 respectively. This difference is significant, but again has the wrong sign to be explicable in terms of convective remixing in the cell. The conditions in the cell used in this work were quite different from those employed by Agar and Turner,[5] who used a cell with a much smaller diameter and much more dilute solutions; both of these factors might tend to favour some remixing by convection, and hence higher Soret coefficients from data obtained exclusively in the early stages of the experiment than from measurements on the system in the steady state. The simplest explanation for the present observations is that equation (2) is not quite adequate except when t approaches infinity. On this view, methods (3) and (4) are the most reliable for the interpretation of beam-displacement data. If this is correct, it is clearly desirable to reduce the duration of the experiments as far as possible by reducing the height of the cell to the lowest practicable value, at least in experiments such as these where the denser component becomes concentrated at the cold wall.

TABLE 3. *Soret coefficients for aqueous* m-*silver nitrate, calculated* (*method* 3) *from results obtained with a modified Tanner cell* (a = 2 mm.).

$\xi_1 = \frac{3}{4}$		$\xi_1 = \frac{1}{2}$		$\xi_1 = \frac{1}{3}$		Whole cell	
Temp. grad. (° c cm.$^{-1}$)	σ (10^{-3} deg.$^{-1}$)	Temp. grad. (°c cm.$^{-1}$)	σ (10^{-3} deg.$^{-1}$)	Temp. grad. (° c cm.$^{-1}$)	σ (10^{-3} deg.$^{-1}$)	Temp. grad. (° c cm.$^{-1}$)	σ (10^{-3} deg.$^{-1}$)
9·95	4·42	9·75	4·35	—	—	9·29	4·36
9·20	4·35	9·76	4·38	—	—	—	—
7·00	4·42	7·17	4·38	7·05	4·40	6·82	4·33
7·02	4·34	7·35	4·35	6·95	4·38	—	—
5·10	4·45	5·05	4·35	4·95	4·36	5·20	4·35
5·02	4·34	5·16	4·42	5·00	4·33	—	—
Mean	4·39	Mean	4·37	Mean	4·37	Mean	4·35

Table 3 shows results obtained with a cell, only 2 mm. in height, in which the steady state was reached in about 20 minutes. It was not possible to use measurements made during the approach to this state principally because the " warming-up " period can no longer be ignored and method (3) is the only practicable one. The deflection at zero time was calculated from the known temperature coefficient of refractive index of the solution derived from measurements in the 10 mm. cell, and the temperature interval from the thermocouple readings corrected for the slight (~1%) temperature loss in the discs described in an earlier section. Obviously, with a cell of this limited height, the accuracy with which ξ_1 could be determined is low, and the relative importance of the finite width of the beam greater than before; neither of these factors, however, should affect the measurement of the infinite time displacement. The results labelled " whole cell " were obtained by omitting the double slit immediately before the cell. The temperature was kept at 25° at the plane explored except in the case of the " whole cell " measurements where this temperature was maintained at the cell centre. There is little difference between the average value of σ for each group of experiments and the mean

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of the 19 results is $4{\cdot}37 \times 10^{-3}$ deg.$^{-1}$ with a standard deviation of the mean of $0{\cdot}01 \times 10^{-3}$ deg.$^{-1}$, a value substantially identical with that obtained on the 10 mm. cell from the second group of experiments recorded in Table 1 for methods (3) and (4). Longsworth's careful study [25] of the same system with a temperature interval of about 10° and a temperature at the cell centre of 25° gave $\sigma = 4{\cdot}27 \times 10^{-3}$ deg.$^{-1}$, which is significantly lower than our values derived from measurements in the steady state, and slightly less than that found by calculation from results obtained during the approach to this state. However, in spite of these differences it is encouraging that two such different methods should give such similar results. The low standard deviation of the mean of the Soret coefficients tabulated in Table 3 arises partly from the large number of observations which the small characteristic time of the 2 mm. cell makes possible. This fact, the satisfactory agreement with the much more laborious experiments carried out in the 10 mm. cell, the smaller risk of convection currents in a cell with a large area : height ratio, and the greater potential sensitivity, make the combination of the optical beam-displacement method with a cell only 2 mm. in height particularly useful.

TABLE 4. *Soret coefficients for more dilute solutions of silver nitrate calculated (method 3) from results obtained from the modified Tanner cell* ($a = 2$ mm.) ($\xi_1 = 0{\cdot}5$, T *at* $\xi = 0{\cdot}5$ *maintained at* 25°. *Temperature gradient* 15° cm.$^{-1}$).

Concn. (molality)	$\sigma \times 10^3$ (deg.$^{-1}$)	
	This work	Longsworth
0·1	3·38	2·84
	3·06 (3·17)	
	3·06	
0·2	3·11	2·89
	3·01 (3·06)	
0·5	3·13	3·23
	3·16 (3·14)	

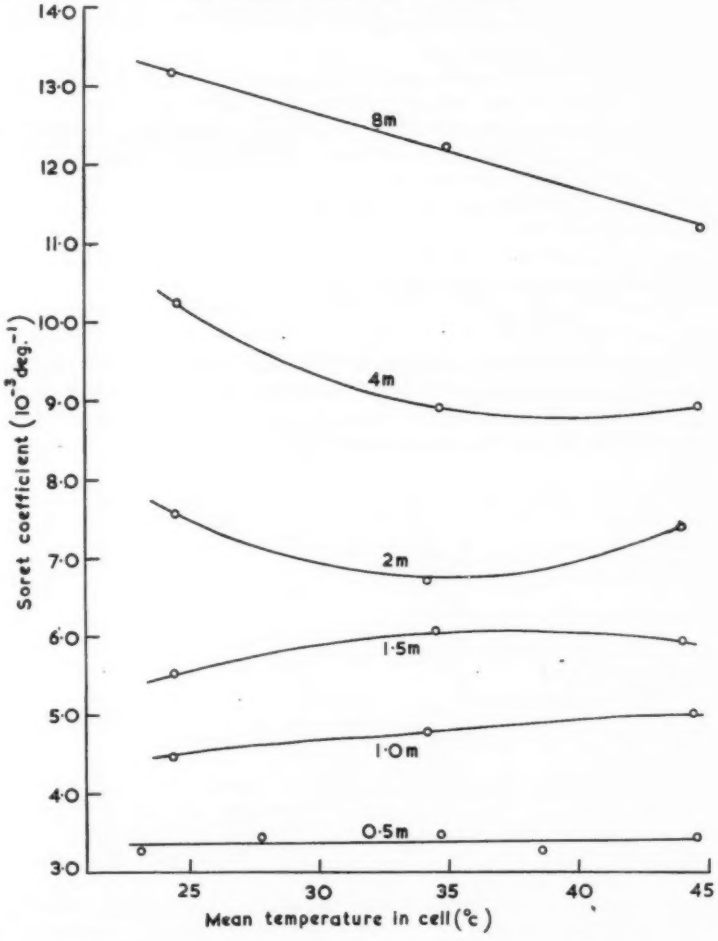
The sensitivity of the apparatus in its present form with the 2 mm. cell can be seen from Table 4 in which results on more dilute solutions of silver nitrate are tabulated and compared with those obtained by Longsworth [25] by the integral-fringe method. The agreement can be considered good, though the accuracy with which the coefficient for the 0·1m-solution could be found was inevitably not very high because of the small proportion of the total beam displacement due to the concentration changes.

Before the necessity for a full analysis of the experimental results was entirely realised, a number of experiments, in which the beam entered at $\xi_1 = \frac{1}{3}$ and the temperature was maintained at the desired value in this plane, were carried out for a wide range of silver nitrate concentrations at several temperatures. While these will not be as accurate as the mean values derived from the results in Tables 2, 3, and 5, their general trend is worth recording here. In Fig. 5 data obtained on the unmodified Tanner cell at 25°, 35°, and 45° are shown for 1—8m-solutions. At the lowest concentrations the Soret coefficient increases with temperature, as is usual for electrolyte solutions, but, at higher concentrations this trend is reversed, a phenomenon which does not seem to have been observed before for an electrolyte solution. Fig. 6 shows the variation of σ with molality at 25°, the data from Tables 2 and 3 being included at the low molality end for comparison. The increase in σ with molality at higher concentrations is characteristic, and there are distinct signs of the minimum which has been observed for a number of electrolyte solutions (cf. ref. 12, chapter 10). When the activity coefficient term $[1 + (\partial \ln \gamma_{\pm}/\partial \ln m)_{T,P}]$ is included and the sum of the ionic entropies of transfer is calculated, the results are rather more striking (Fig. 7). There is a clear minimum at about 0·5m and a steep rise thereafter up to 2m. Above this concentration it falls off slightly to the highest concentration studied. The initial fall in the entropy of transfer with increasing concentration observed for all electrolytes studied in sufficiently dilute solution has been explained by Agar,[4] but a

detailed explanation of the changes at higher concentrations is not at present possible. In any event this would be complicated for silver nitrate solutions by the ion association which occurs.

Conclusions.—(1) The available solutions of the diffusion equation for a pure Soret effect cell, when expressed in an easily usable form, give reasonably satisfactory representations of optical beam-displacement measurements on m-silver nitrate. They are not,

FIG. 5. *Variation of the Soret coefficient of aqueous silver nitrate solutions with mean cell temperature. (Unmodified Tanner cell, a = 10 mm.)*



however, completely satisfactory for this purpose, since Soret coefficients calculated from measurements in the early stages of the experiment vary significantly with the position of the exploring beam in the cell and with the magnitude of the temperature gradient. Similar coefficients calculated from steady-state measurements alone varied much less.

(2) Mean values of such coefficients, obtained from experiments on m-silver nitrate in which the cell was explored at planes disposed approximately symmetrically above and below the centre, and calculated from the rate of attainment of the steady-state

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equilibrium, were slightly lower ($4{\cdot}31 \times 10^{-3}$ deg.$^{-1}$) than the similar mean coefficients calculated from steady-state data. Almost identical values ($4{\cdot}38$, $4{\cdot}37 \times 10^{-3}$ deg.$^{-1}$) for these coefficients were obtained from experiments on cells having $a = 10$ mm. and 2 mm. respectively. All these values are slightly higher than that obtained ($4{\cdot}27 \times 10^{-3}$ deg.$^{-1}$) for the same system at the same mean temperature (25°) by Longsworth who used an integral-fringe method.

(3) It has been shown that accurate measurements can be made rapidly on a cell with

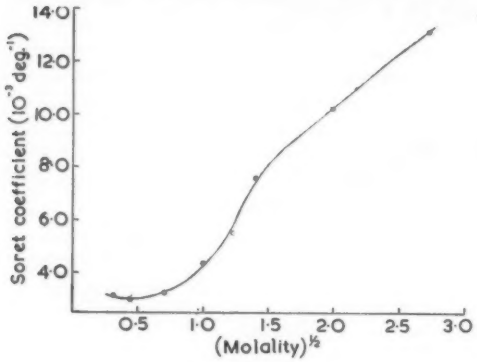


FIG. 6. *Variation of the Soret coefficient of aqueous silver nitrate with molality at a mean cell temperature of* 25°.

a plate separation of 2 mm., the results being identical with those obtained, with much greater labour, on a cell with the more usual separation of 10 mm. In addition, the sensitivity of the beam-displacement method then matches that of the integral-fringe arrangements without the use of large temperature intervals.

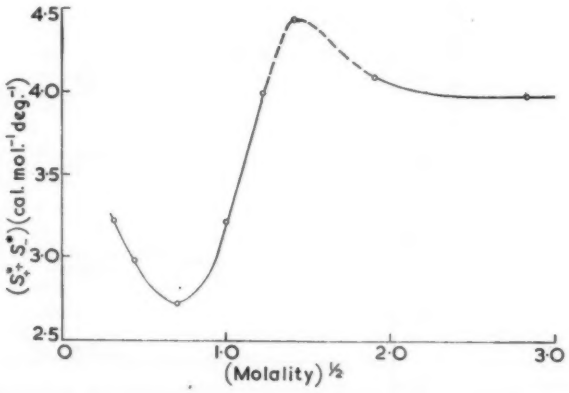


FIG. 7. $(S_+^* + S_-^*)$ *for aqueous* 0·1—8m-*silver nitrate at* 25°.

(4) Approximate results obtained for silver nitrate solutions up to 8 molal have shown the interesting variations in σ and $(S^*_+ + S^*_-)$ for this system with changes in concentration and mean temperature, though these are at present not explicable in terms of the structure of the solution.

We are indebted to Dr. C. C. Tanner for the gift of his Soret effect cell, and to the Department of Scientific and Industrial Research for the award of a maintenance grant to one of us (J. G. F.).

THE UNIVERSITY, SHEFFIELD. [*Received, March* 1*st*, 1961.]

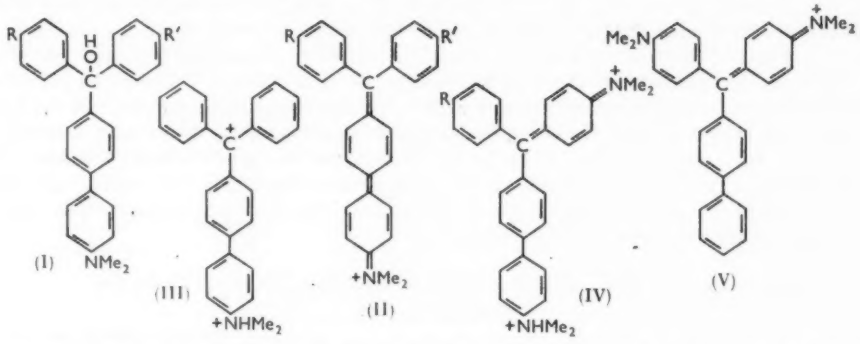
668. *Steric Effects in Di- and Tri-arylmethanes. Part VII.* Biphenyl Analogues of Crystal Violet and Malachite Green.*

By C. C. Barker and A. Stamp.

Spectral studies show that terminal nitrogen atoms attached to biphenyl groups in analogues of Crystal Violet and Malachite Green have little tendency to conjugate with the central carbon atom. Conjugation is most effective in the Crystal Violet analogue (II; R = R′ = NMe_2) in which a high resonance energy counterbalances the high energy of the quinonoid biphenyl group.

In previous papers of this series the spectral changes brought about in basic di- and triphenylmethane dyes by twisting groups about central and terminal bonds have been discussed. Biphenyl analogues of these dyes appeared to provide an opportunity to study the effect of twisting the dye molecules about an intermediate bond.

One equivalent of perchloric acid with (4′-dimethylamino-4-biphenylyl)diphenylmethanol (I; R = R′ = H) in acetic acid protonates the dimethylamino-group [1] instead of forming the ion (II; R = R′ = H); more perchloric acid then gives the coloured protonated carbonium ion (III). The extended quinonoid system in (II) appears to be energetically unfavourable but this effect can be offset by resonance stabilisation in analogous di- and tri-aminotriarylmethane dyes. Thus, bis-(4′-dimethylamino-4-biphenylyl)phenylmethanol (I; R = H, R′ = p-$Me_2N{\cdot}C_6H_4$) in hot acetic acid gives a weak green colour which fades reversibly on cooling; adding concentrated formic, perchloric, or sulphuric acid gives the red protonated carbonium ion.[2] Maximum stabilisation of the



quinonoid biphenyl system should be achieved in the biphenylyl analogues of Crystal Violet, in particular, the monobiphenylyl analogue (II; R = R′ = NMe_2), the spectrum of which was therefore examined. Effective conjugation of the nitrogen atom attached to the biphenylyl group with the central carbon atom in this dye would result in a spectrum with a single band in the visible region (cf. Crystal Violet) whereas absence of conjugation, and subsequent protonation of the nitrogen atom, would result in a strong first frequency band and a weak second frequency band in the visible region (cf. Malachite Green). The closest approach to the spectrum of the univalent ion (II; R = R′ = NMe_2) is obtained from the dye base in ethanol with 1 equivalent of hydrogen chloride (Fig.) but the second frequency band ($\varepsilon_{max.}$ 8000) indicates the presence of approximately 28% of the bivalent cation (IV; R = NMe_2) and the observed value of $\lambda_{max.}$ (617·5 mμ) is therefore higher than

* Part VI, *J.*, 1961, 2642.

[1] Morton and Wood, *J. Amer. Chem. Soc.*, 1939, **61**, 2902.
[2] Theilacker and Schmid, *Chem. Ber.*, 1951, **84**, 204.

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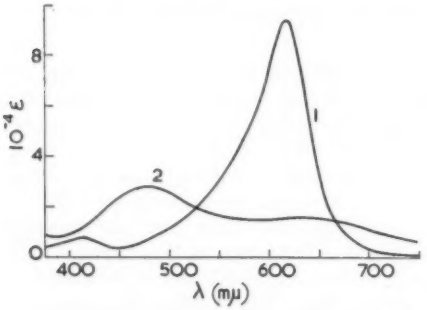
that of the univalent ion, but it is very probable that this ion absorbs at longer wavelength than Crystal Violet (589 mμ) and that the bathochromic shift is due to the more extended conjugation of the biphenyl system.

In 90% acetic acid or in 98% acetic acid with 12·5 equivalents of hydrogen chloride ($10^{-4} \times 1{\cdot}15$M) a close approximation to the spectrum of the bivalent ion (IV; R = NMe_2) is obtained, this being shown by the correspondence between the intensity of the second band ($\varepsilon_{max.}$ 29,000) and the intensity of the second band of the 4-phenyl derivative of Malachite Green (V; $\varepsilon_{max.}$ 30.000) (Table).



Absorption spectra of (1) *(4′-dimethylamino-4-biphenylyl)bis-(4-dimethylaminophenyl)methanol in ethanol with* 1 *equiv. of hydrochloric acid, and* (2) *(4′-dimethylamino-4-biphenylyl)-4-dimethylaminodiphenylmethanol in acetic acid.*

The biphenylyl analogue of Malachite Green base (I; R = H, R′ = NMe_2) shows much less tendency to form a univalent cation than the corresponding analogue of Crystal Violet base (I; R = R′ = NMe_2). Thus, in pure acetic acid the first band of the univalent ion (II; R = H, R′ = NMe_2) is of low intensity ($\varepsilon_{max.}$ less than 20,000 as compared with 104,000 observed with Malachite Green) and merges without a well-defined maximum into the first band of the bivalent ion (IV; R = H), $\lambda_{max.}$ 476·5 mμ, ε 28,000 (Fig.). In 90% acetic acid the intensity of the long-wavelength band is reduced below 5000, and the intensity of the second band increases to 32,000, a value comparable with that of the first band of the closely related *NN*-dimethylfuchsonimonium ion ($\lambda_{max.}$ 465·5 mμ; ε 35,000). In ethanol with one equivalent of hydrogen chloride the base gives a first band which is more intense than the second band (Table), but both of the bands fade rapidly and the absolute values of the intensities are not significant. This fading is probably due to the formation of the ethyl ether of the dye base.

Spectral data for 10^{-5}M-*solutions of biphenyl analogues of Crystal Violet and Malachite Green.*

Dye	Solvent	Absorption maxima (mμ) ($10^{-4}\varepsilon$ in parentheses)
Crystal Violet	98% HOAc	589 (11·6)
(II; R = R′ = NMe_2)	100% HOAc	621 (10·4); 448·5 (1·4)
,, ,,	98% HOAc	622·5 (10·1); 446 (2·0)
,, ,,	90% HOAc	627·5 (9·6); 444·5 (2·6)
,, ,,	98% HOAc + 12·5 equiv. HCl	626 (9·6); 445·5 (2·9)
,, ,,	EtOH + 1 equiv. HCl	617·5 (9·4); 415 (0·8)
Malachite Green	98% HOAc	621 (10·4); 427·5 (2·0)
(II; R = H, R′ = NMe_2)	100% HOAc	476·5 (2·8)
,, ,,	90% HOAc	476·5 (3·2)
,, ,,	EtOH + 1 equiv. HCl	625 (0·4); 463 (0·3) *
V	98% HOAc	623·5 (10·0); 453·5 (3·0)

* Bands faded rapidly.

Thus, it is likely that, even in the most favourable case of the monobiphenylyl analogue of Crystal Violet, twisting part of the molecule about the intermediate bond would lead to such a low concentration of ions containing the remote nitrogen atom conjugated with the central carbon atom that little useful spectroscopic information would be

obtained. The difficulty with which the mesomeric effect is transmitted through the biphenylyl system in these basic dyes is surprising in view of the spectroscopic evidence showing effective conjugation of the terminal groups in 4-amino-4′-nitrobiphenyl [3] and in the (4′-methoxy-4-biphenylyl)diphenylmethyl ion.[4] The increased intensity of the *y*-band of the 4-phenyl derivative of Malachite Green (V) ($\varepsilon_{max.}$ 30,000) implies effective conjugation of the remote phenyl group (cf. the *y*-band of the 4-methoxy-derivative of Malachite Green, $\varepsilon_{max.}$ 34,000), but in this case charge is not localised to the extent that it is when a terminal nitrogen atom is conjugated with the central carbon atom through the biphenylyl system.

Preparations.—The use of 4-bromo- and 4-iodo-4′-dimethylaminobiphenyl to prepare the dye bases is complicated by difficulty in converting these halides into lithium or Grignard compounds [2] but Rodd and Linch's method,[5] which involves condensing a diaryl ketone with aryl halide in the presence of sodium, is satisfactory. Thus, 4′-dimethylaminobiphenylyl-lithium, from 4-bromo-4′-dimethylaminobiphenyl and butyl-lithium, gives impure (4′-dimethylamino-4-biphenylyl)bis-(4-dimethylaminophenyl)methanol (I; R = R′ = NMe_2) with Michler's ketone, but this ketone with 4-dimethylamino-4′-iodobiphenyl and sodium gives the pure base. Also, attempts to repeat the preparation of bis-(4′-dimethylamino-4-biphenylyl)phenylmethanol (I; R = H, R′ = *p*-$Me_2N{\cdot}C_6H_4$) from 4-dimethylamino-4′-biphenylylmagnesium iodide [2] and ethyl benzoate gave impure material whereas 4-(4-dimethylaminophenyl)benzophenone with 4-dimethylamino-4′-iodobiphenyl and sodium gives the pure base. On the other hand, 4-dimethylamino-4′-iodobiphenyl with 4-dimethylaminobenzophenone and sodium gives slightly impure (4′-dimethylamino-4-biphenylyl)-4-dimethylaminodiphenylmethanol (I; R = H, R′ = NMe_2) whereas 4-dimethylaminophenyl-lithium with 4-(4-dimethylaminophenyl)benzophenone gives pure base.

The 4-phenyl derivative of Malachite Green base, obtained by the interaction of 4-chlorobiphenyl, Michler's ketone and sodium, gives a first band ($\varepsilon_{max.}$ 100,000) which is a little weaker than is usual with 4-substituted derivatives of Malachite Green ($\varepsilon_{max.}$ 104,000—108,000), but purification by reduction to the leuco-compound followed by oxidation, or synthesis from 4-biphenylyl-lithium and Michler's ketone gives material showing a first band of the same intensity.

Experimental

4-Bromo-4′-dimethylaminobiphenyl.—A mixture of 4-amino-4′-bromobiphenyl (47·0 g.) and trimethyl phosphate (14·9 c.c.) was kept at 170—180° for 20 min. and then at 190—200° for 2 hr. The mixture was boiled for 1·5 hr. with aqueous sodium hydroxide (26·5 g. in 200 c.c.), water (300 c.c.) was then added, and the crude product was sublimed at reduced pressure and then kept at 100° for 30 min. in pyridine (160 c.c.) containing succinic anhydride (16·7 g.). The mixture was then poured into an excess of aqueous 2N-sodium hydroxide, and the precipitate was crystallised from benzene (250 c.c.) giving 4-bromo-4′-dimethylaminobiphenyl (35·5 g.), m. p. 209—210°; Banus and Medrano [6] give m. p. 209—211°.

4-(4-Dimethylaminophenyl)benzophenone.—Butyl-lithium (0·2 mole) was added to 4-bromo-4′-dimethylaminobiphenyl (5·52 g.) in benzene (200 c.c.), the mixture kept for 1 hr. and then cooled in ice, and benzonitrile (20·6 g.) added. After a further 1 hr. the mixture was poured into water, and concentrated hydrochloric acid was added until the solution was colourless. The aqueous layer was boiled for 1 hr. and then basified with ammonia (*d* 0·88). The dried precipitate, twice crystallised from 2 : 1 benzene–ethanol gave yellow leaflets of *4-(4-dimethylaminophenyl)benzophenone* (3·1 g.), m. p. 184—185° (Found: C, 84·1; H, 6·5; N, 4·5. $C_{21}H_{19}NO$ requires C, 83·8; H, 6·3; N, 4·7%).

(4′-Dimethylaminobiphenyl)-4-dimethylaminodiphenylmethanol.—4-Dimethylaminophenyl-lithium in ether, from 4-bromo-*NN*-dimethylaniline (1·4 g.), was added under nitrogen to a

[3] Jones, *J. Amer. Chem. Soc.*, 1952, **74**, 5074.
[4] Anderson and Fisher, *J. Amer. Chem. Soc.*, 1944, **66**, 594.
[5] Rodd and Linch, *J.*, 1927, 2174.
[6] Banus and Medrano, *Anales real Soc. espan. Fis. Quim.*, 1922, **20**, 477.

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suspension of 4-(4-dimethylaminophenyl)benzophenone (1·0 g.) in ether (50 c.c.). The mixture was kept for 2 hr. and then poured into water. Ether was removed from the dried (Na_2SO_4) organic layer, and the residue was twice crystallised from ethanol and then chromatographed in benzene on alumina, those eluates which gave a red colour in acetic acid being retained. The residue from these eluates, when crystallised from ethanol, gave the required *base* (0·3 g.), m. p. 119—120·5° (Found: C, 82·0; H, 7·3; N, 6·4. $C_{29}H_{30}N_2O$ requires C, 82·4; H, 7·2; N, 6·6%).

Bis-(4′-dimethylamino-4-biphenylyl)phenylmethanol.—A well-stirred mixture of 4-(4-dimethylaminophenyl)benzophenone (1·0 g.), 4-dimethylaminophenyl-4′-iodobiphenyl (1·17 g.), sodium (0·17 g.), and benzene (25 c.c.) was boiled under nitrogen for 24 hr. Water was then added and the residue from the dried (Na_2SO_4) benzene layer, after three crystallisations from toluene, gave the required base (0·9 g.), m. p. 225—226° (lit.,[2] 214—216°) (Found: C, 84·3; H, 6·9; N, 5·3. Calc. for $C_{35}H_{34}N_2O$: C, 84·3; H, 6·9; N, 5·6%).

(4′-Dimethylamino-4-biphenylyl)bis-(4-dimethylaminophenyl)methanol.—The interaction of 4-dimethylamino-4′-iodobiphenyl (2·35 g.), Michler's ketone (1·85 g.), and sodium (0·35 g.) under the conditions used in the previous preparation, and two crystallisations from ethanol, gave the required *base* (0·9 g.), m. p. 179—180° (Found: C, 79·9; H, 7·6; N, 8·9. $C_{31}H_{35}N_3O$ requires C, 79·9; H, 7·6; N, 9·0%).

αα-Bis(4-dimethylaminophenyl)-4-biphenylylmethyl Methyl Ether.—The interaction of 4-chlorobiphenyl (9·5 g.), Michler's ketone (13·4 g.), and sodium (2·3 g.) under conditions used in the previous preparation yielded, after two crystallisations from ethanol, *αα-bis-(4-dimethylaminophenyl)biphenylylmethanol* (11·3 g.), m. p. 152—153° (Found: C, 82·4; H, 7·4; N, 6·5. $C_{29}H_{30}N_2O$ requires C, 82·4; H, 7·2; N, 6·6%). To this base (2·0 g.) in dilute hydrochloric acid was added zinc dust until a drop of the solution gave no colour with sodium acetate. Basification of the solution with aqueous ammonia gave *αα-bis-(4-dimethylaminophenyl)biphenylylmethane* (1·2 g.), m. p. 189—189·5° (from 1 : 1 ethanol–benzene) (Found: C, 85·8; H, 7·4; N, 6·8. $C_{29}H_{30}N_2$ requires C, 85·7; H, 7·4; N, 6·9%). A mixture of this base (1·15 g.), chloranil (0·76 g.), and methanol (30 c.c.) was boiled for 30 min. The filtered solution was reduced to 15 c.c. and then poured into methanol (10 c.c.) containing sodium methoxide (0·4 g.), giving a precipitate of the *methyl ether* (1·0 g.), m. p. 147—148° (thrice crystallised from 2 : 1 methanol–benzene) (Found: C, 82·8; H, 7·3; N, 6·5. $C_{30}H_{32}N_2O$ requires C, 82·5; H, 7·4; N, 6·4%).

One of us (A. S.) thanks the Hull Education Authority for a grant.

THE UNIVERSITY, HULL. [*Received, December 22nd,* 1960.]

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669. *Organic Fluorine Compounds. Part XX.* Some Reactions of 1-Chloro-3-fluoropropan-2-ol and Epifluorohydrin.*

By ERNST D. BERGMANN, SASSON COHEN, and ISRAEL SHAHAK.

In 1-chloro-3-fluoropropan-2-ol the chlorine atom is much more prone to nucleophilic attack than the fluorine. The reactions with potassium cyanide, sodium ethoxide, and sodium phenoxide have been studied. Also in epifluorohydrin the oxide ring is opened by diethyl sodiomalonate without attack on the fluorine atom. Alkyl- and aryl-magnesium bromide with epifluorohydrin give 1-bromo-3-fluoropropan-2-ol; phenyl-lithium gives 1-fluoro-3-phenylpropan-2-ol.

The preparation of alkyl fluorolactates and fluoropyruvates is described.

THE easy availability, from epichlorohydrin, of 1-chloro-3-fluoropropan-2-ol and epifluorohydrin [1,2] has led us to study the reactions of these compounds. The publication of similar experiments by Cherbuliez and his co-workers [3] prompts us to report our results.

* Part XIX, Bergmann and Shahak, *J.*, 1960, 5261.

[1] Bergmann and Cohen, *J.*, 1958, 2259.
[2] Pattison and Norman, *J. Amer. Chem. Soc.*, 1957, **79**, 2311.
[3] Cherbuliez, Yazgi, and Rabinowitz, *Helv. Chim. Acta*, 1960, **43**, 1135; Cherbuliez, de Picciotto, and Rabinowitz, *ibid.*, p. 1143.

The chlorine atom in 1-chloro-3-fluoropropan-2-ol is, as expected, much more reactive than the fluorine towards nucleophilic reagents. Sodium cyanide yields γ-fluoro-β-hydroxybutyronitrile; the yield is somewhat better than that reported for the reaction with potassium cyanide. This nitrile was converted by reaction with ethanol and hydrogen chloride into the corresponding ethyl ester and the latter dehydrated with phosphorus pentoxide to ethyl γ-fluorocrotonate. With sodium ethoxide and sodium phenoxide, the chloropropanol was converted into 1-ethoxy-3-fluoro- and 1-fluoro-3-phenoxy-propan-2-ol, respectively, which were then oxidised to the disubstituted acetones.

Analogously, the ethylene oxide ring in epifluorohydrin is more open to nucleophilic attack than the fluorine atom. Cherbuliez *et al.*[3] have already described, *inter alia*, the reaction with dimethylamine which ultimately led to *N*-acetyl-2-fluoromethylcholine. In addition to this reaction, which we carried out in almost the same way, we observed that diethyl sodiomalonate gives δ-fluoro-γ-valerolactone after acid hydrolysis of the primary product. This reaction is analogous to that of ethylene oxides in general, including epichlorohydrin.[4]

With methyl-, butyl-, or phenyl-magnesium bromide, 1-bromo-3-fluoropropan-2-ol was obtained; only in the case of phenylmagnesium bromide a small amount of the expected 1-fluoro-3-phenylpropan-2-ol was secured. When phenyl-lithium was used at −70°, a 52% yield of the phenylpropanol was obtained.

As to the formation of 1-bromo-3-fluoropropan-2-ol, the mechanism of such reactions with ethylene oxides have been discussed by Kharasch and Reinmuth; [5] as to the reaction with phenyl-lithium, it is worthy of note that epichlorohydrin with phenylmagnesium bromide also gives, together with 1-bromo-3-chloropropan-2-ol, 1-chloro-3-phenylpropan-2-ol,[6] and with butyl-lithium gives 1-chlorohexan-2-ol.[7]

The preparation of 1-fluoropropane-2,3-diol from epifluorohydrin and its oxidation to 3-fluorolactic acid with nitric acid,[2] in analogy with the known preparation of 3-chlorolactic acid,[8] have been described before. However, the fluorolactic acid can be prepared more easily if the diol is replaced by the isopropylidene derivative, which is obtained in excellent yield from glycerol.[9] 3-Fluorolactic acid is most easily isolated from the reaction product as its ethyl or butyl ester.

Ethyl 3-fluorolactate can be converted into ethyl fluoropyruvate by reaction with *N*-bromosuccinimide (1 mole); with an excess of this reagent, ethyl bromofluoropyruvate is obtained, in analogy to the formation of ethyl bromopyruvate from ethyl lactate.[10] It is worthy of note that both ethyl fluoropyruvate and bromofluoropyruvate give, with 2,4-dinitrophenylhydrazine, the osazone of ethyl mesoxaldehydate.[11] In the former case, the reaction is the same as for the 2-hydroxycarbonyl compounds; under appropriate conditions, the normal 2,4-dinitrophenylhydrazone of ethyl fluoropyruvate can be obtained.

Experimental

γ-Fluoro-β-hydroxybutyronitrile.—A stirred mixture of 1-chloro-3-fluoropropan-2-ol (40 g.), sodium cyanide (18 g.), and water (10 g.) was heated at 50—60° for 2 hr. To the cooled solution, a large excess of acetone was added and the filtered solution distilled. The *nitrile* (18 g., 49%) boiled at 125—128°/15 mm. (Found: C, 46·1; H, 6·4; F, 18·1. C_4H_6FNO requires C, 46·6; H, 5·8; F, 18·4%).

[4] Traube and Lehmann, *Ber.*, 1899, **32**, 720; 1901, **34**, 1971; Haller, *Bull. Soc. chim. France*, 1899, **21**, 564; *Compt. rend.*, 1906, **142**, 1471.
[5] Kharasch and Reinmuth, "Grignard Reactions of Non-metallic Substances," Prentice-Hall Inc., New York, 1954, p. 961.
[6] Fourneau and Tiffeneau, *Bull. Soc. chim. France*, 1907, **1**, 1227.
[7] Gilman, Hofferth, and Honeycutt, *J. Amer. Chem. Soc.*, 1952, **74**, 1594.
[8] Koelsch, *J. Amer. Chem. Soc.*, 1930, **52**, 1105.
[9] Bergmann and Shahak, *Chem. and Ind.*, 1958, 157.
[10] Stuckwisoh, Hammer, and Blau, *J. Org. Chem.*, 1957, **22**, 1678.
[11] Bergmann and Shahak, *J.*, 1960, 462, 3225.

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Ethyl γ-Fluoro-β-hydroxybutyrate.—A slow stream of hydrogen chloride was passed for 1 hr. through a boiling mixture of the foregoing compound (33 g.), 95% ethanol (33 g.), and water (3·5 ml.). To the cooled solution, an excess of ether was added. After 6 hr. the ammonium chloride was filtered off and the ethereal solution distilled. The *ester* (32 g., 67%) boiled at 104—108°/18 mm. (Found: C, 47·8; H, 7·0. $C_6H_{11}FO_3$ requires C, 48·0; H, 7·3%).

Ethyl γ-Fluorocrotonate.—Phosphorus pentoxide (10 g.) was added in small portions to a solution of the hydroxy-ester (16 g.) in benzene (30 ml.), and the mixture refluxed for 15 min. The benzene solution was decanted from the brown precipitate and distilled. The *ester* (7 g., 50%) boiled at 66—67°/21 mm. (Found: C, 54·8; H, 6·8. $C_6H_9FO_2$ requires C, 54·5; H, 6·8%).

1-*Ethoxy*-3-*fluoropropan*-2-*ol.*—1-Chloro-3-fluoropropan-2-ol (25 g.) was refluxed in 2N-ethanolic sodium ethoxide (100 ml.) for 2 hr., filtered, and distilled. The *product* (6 g., 22%) had b. p. 71—72°/28 mm. and n_D^{29} 1·3995 (Found: C, 49·5; H, 9·0; F, 15·4. $C_5H_{11}FO_2$ requires C, 49·2; H, 9·0; F, 15·6%).

1-*Ethoxy*-3-*fluoroacetone.*—To a mixture of the foregoing alcohol (31 g.), sodium dichromate (41·5 g.), and water (70 ml.), a mixture of concentrated sulphuric acid (69·5 g.) and water (20 ml.) was added at 15—20° with stirring. After 2 hr. the solution was extracted with ether, and the ethereal solution dried and distilled. The *ketone* (18 g., 58%) boiled at 63—65°/25 mm. (Found: C, 50·0; H, 7·4; F, 15·9. $C_5H_9FO_2$ requires C, 50·0; H, 7·5; F, 15·8%).

1-*Fluoro*-3-*phenoxypropan*-2-*ol.*—During 3 hr., a mixture of 1-chloro-3-fluoropropan-2-ol (23 g.), phenol (19 g.), and sodium hydroxide (8·5 g.) in water (70 ml.) was refluxed. The product was extracted with ether, and the ethereal solution dried and distilled twice. The new *alcohol* (28 g., 89%) boiled at 110—111°/4 mm. and had n_D^{30} 1·5138 (Found: F, 11·2. $C_9H_{11}FO_2$ requires F, 11·2%).

1-*Fluoro*-3-*phenoxyacetone.*—To a solution of the foregoing compound (24 g.) in acetone (70 ml.), a mixture of chromic anhydride (15 g.), concentrated sulphuric acid (23 g.), and water (40 ml.) was added at 15—20°. After 3 hr. an excess of water was added and the product extracted with ether. The slightly yellow *ketone* (17 g., 68%) had b. p. 115—117°/4 mm. and n_D^{28} 1·5125 (Found: C, 63·6; H, 6·0; F, 11·7. $C_9H_9FO_2$ requires C, 64·3; H, 5·4; F, 11·3%).

δ-*Fluoro*-γ-*valerolactone.*—To a solution prepared from sodium (12 g.), ethanol (250 ml.) and diethyl malonate (80 g.), epifluorohydrin (38 g.) was added. After 2 hr. at 40—50°, the viscous product was poured into ice and hydrochloric acid. The solution was concentrated *in vacuo* and the concentrate extracted with ether. The extract was evaporated and the residue refluxed with 10% aqueous hydrochloric acid (100 ml.) for 5 hr.; the aqueous acid was distilled off *in vacuo* and the residue fractionated, giving the *lactone* (18 g., 33%), b. p. 127—129°/32 mm., n_D^{27} 1·4260 (Found: C, 50·6; H, 6·0; F, 16·0. $C_5H_7FO_2$ requires C, 50·8; H, 6·0; F, 16·1%).

1-*Fluoro*-3-*phenylpropan*-2-*ol.*—At −70°, and with stirring, a phenyl-lithium solution, prepared from lithium (4 g.) and bromobenzene (44 g.) in ether (100 ml.), was added during 30 min. to a solution of epifluorohydrin (19 g.) in ether (50 ml.). The temperature was raised to 0° in 2 hr. and the product poured into ice and dilute sulphuric acid. The *alcohol* (20 g., 52%) boiled at 115—120°/15 mm. (Found: C, 69·8; H, 7·0. $C_9H_{11}FO$ requires C, 70·1; H, 7·1%).

1-*Bromo*-3-*fluoropropan*-2-*ol.* Epifluorohydrin (14 g.) was added, dropwise and with stirring, to a Grignard solution [from magnesium (2·4 g.), bromobenzene (16 g.) and ether (120 ml.)] at 0°. The solution was stirred for 1 hr., then poured on ice and concentrated sulphuric acid (10 ml.). The ethereal layer was separated and the aqueous phase extracted three times with ether. The combined ether extracts were dried (Na_2SO_4) and gave, on distillation, fractions (*a*) 1-bromo-3-fluoropropan-2-ol, b. p. 78—80°/30 mm. (7·5 g., 27% based on epifluorohydrin), and (*b*) 1-fluoro-3-phenylpropan-2-ol, b. p. 125—130°/30 mm. (4·5 g., 16% based on epifluorohydrin), identical with the product obtained in the preceding experiment.

Ethyl and Butyl 3-*Fluorolactate from* 4-*Fluoromethyl*-2,2-*dimethyl*-1,3-*dioxolan.*—A mixture of this isopropylidene derivative[9] (67 g.), water (80 ml.), and concentrated hydrochloric acid (20 ml.) was gradually heated, with stirring, to 80—90°. At this point, an exothermic reaction set in, and the liquid became homogeneous. The mixture was refluxed for 20 min., then distilled through a Vigreux column until 60 ml. of distillate had collected. After dilution of the residue with water (100 ml.), a mixture of 70% nitric acid (140 ml.) and water (100 ml.) was added, with stirring, at such a rate that the temperature did not exceed 60° (5 hr.). The solution was left at room temperature for 48 hr., heated at 60° for 1 hr., and concentrated at 60°/30—40 mm. After addition of water (100 ml.), the distillation was repeated and continued to dryness. The remaining syrup is fluorolactic acid of 90—95% purity.

The syrup was distilled azeotropically with anhydrous ethanol (50 g.), benzene (150 ml.), and toluene-*p*-sulphonic acid (0·5 g.). When no more water collected, part of the solution (50 ml.) was distilled off through a Vigreux column and the residue neutralised with sodium hydrogen carbonate (5 g.), filtered, freed from solvents, and distilled at 30 mm. Ethyl fluorolactate (31—38 g., 45—56%) boiled at 96—98°/30 mm. It is colourless, water-soluble, and very quickly hydrolysed in water (Found: C, 44·3; H, 6·7; F, 13·7. Calc. for $C_5H_9FO_3$: C, 44·1; H, 6·6; F, 14·0%).

In the same manner, *butyl fluorolactate* (59 g., 72%) was obtained; it had b. p. 94—95°/3 mm. (Found: C, 51·1; H, 7·7; F, 11·3. $C_7H_{13}FO_3$ requires C, 51·2; H, 7·9; F, 11·6%).

2-Ethyl-4-hydroxymethyl-2-methyl-1,3-dioxolan.—Azeotropic condensation of glycerol (500 g.) and ethyl methyl ketone (430 g.) in benzene (500 ml.) in the presence of toluene-*p*-sulphonic acid (20 g.) was carried out with vigorous agitation. The resulting solution was washed with sodium carbonate solution and water, dried, and distilled. The *product* (700 g., 80%) boiled at 72—73°/2 mm. or 126—128°/30 mm. (Found: C, 57·8; H, 9·4. $C_7H_{14}O_3$ requires C, 57·5; H, 9·6%).

2-Ethyl-4-fluoromethyl-2-methyl-1,3-dioxolan.[9]—The foregoing product was converted into the toluene-*p*-sulphonate, with benzene as reaction medium instead of ethanol,[12] as follows: The hydroxymethyl compound (146 g.) in benzene (100 ml.) was added slowly and with stirring to a suspension of sodium hydride (24 g.) in benzene (600 ml.). The mixture was refluxed for 30 min. and at 25° toluene-*p*-sulphonyl chloride (190 g.) in benzene (300 ml.) added with stirring. When the organic chloride had disappeared (test with alcoholic silver nitrate solution), the mixture was poured into cold water, and the benzene layer dried and concentrated *in vacuo* (first 10, then 1 mm.) at $\gtrsim$80°. The toluene-*p*-sulphonate (quantitative yield) formed an oil which could not be distilled without decomposition and was used in its crude state for the fluorination.

In a 3-necked one-litre flask, fitted with stirrer, bent condenser, dropping funnel, gas-inlet, and thermometer, the toluene-*p*-sulphonate (300 g.) was added to a mixture of carefully dried potassium fluoride (90 g.) and anhydrous diethylene glycol (300 ml.), and the mass heated quickly until reaction set in, and then brought slowly to 150°. After 5 min. at this temperature, a current of air was passed through the mass for 10 min. The distillate was dissolved in ether and washed successively with 10% hydrochloric acid, sodium hydrogen carbonate solution, and water. Distillation of the dried product gave at 146—147°/760 mm. the fluorine compound (123 g., 84%; larger batches gave somewhat lower yields) (Found: C, 56·9; H, 8·7; F, 12·5. Calc. for $C_7H_{13}FO_2$: C, 56·8; H, 8·8; F, 12·8%).

Ethyl Fluoropyruvate from Ethyl Fluorolactate.—A mixture of ethyl fluorolactate (20·4 g.), *N*-bromosuccinimide (26·7 g.), and carbon tetrachloride (150 ml.) was refluxed for 1 hr. The cold solution was filtered and distilled in a short column. The ester (4·5 g., 22·5%) boiled at 82—83°/25 mm. (Found: C, 45·0; H, 5·4; F, 14·1. Calc. for $C_5H_7FO_3$: C, 44·8; H, 5·2; F, 14·2%).

Reaction with 2,4-dinitrophenylhydrazine gave first *ethyl fluoropyruvate 2,4-dinitrophenylhydrazone*, m. p. 125—126° (from dilute alcohol) (Found: C, 42·3; H, 3·8; F, 6·0; N, 17·5; OEt, 13·7. Calc. for $C_{11}H_{11}FN_4O_6$: C, 42·0; H, 3·5; F, 6·1; N, 17·5; OEt, 14·3%). This was converted, especially at elevated temperature, into the ethyl mesoxaldehydate osazone, m. p. 250° (from acetic acid) (Found: C, 41·8; H, 3·0; N, 22·4. Calc. for $C_{17}H_{14}N_8O_{10}$: C, 41·6; H, 2·8; N, 22·8%).

Ethyl Bromofluoropyruvate from Ethyl Fluorolactate.—A mixture of ethyl fluorolactate (20·4 g.), *N*-bromosuccinimide (53·5 g.), and carbon tetrachloride (250 ml.) was refluxed for 2 hr., then filtered, and the solution distilled. The ester (8 g., 25%) boiled at 100—101°/40 mm. (Found: C, 28·4; H, 3·1; F, 8·6. Calc. for $C_5H_6BrFO_3$: C, 28·2; H, 2·8; F, 8·9%). With 2,4-dinitrophenylhydrazine this gave ethyl mexosaldehydate osazone, m. p. 250°.

Infrared Spectra (Liquid Film).[13]—In epifluorohydrin, the fluorine bands were observed at 1020 and 1120, the nitrile band at 2300, and the hydroxyl peak at 3500 cm.$^{-1}$. For ethyl γ-fluoro-β-hydroxybutyrate, the following assignments were made: 3430 (OH), 1760 (ester C=O), 1100, 1015 cm.$^{-1}$ (C–F). For ethyl γ-fluorocrotonate, the carbonyl peak is shifted to 1705 cm.$^{-1}$; in the C–F region, there appear strong bands at 1033, 1085, and 1170 cm.$^{-1}$; the double bond absorbs at 1660 cm.$^{-1}$.

[12] Fichter and Schoenmann, *Helv. Chim. Acta*, 1936, **19**, 1411.
[13] For the C–F stretching frequency, see, *e.g.*, Klaboe and Nielsen, *J. Chem. Phys.*, 1960, **32**, 899.

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The following bands were also allotted:

1-Ethoxy-3-fluoropropan-2-ol: 3400 (OH); in the C–F and C–O–C region: 1020 and 1085 cm.$^{-1}$.

1-Fluoro-3-phenoxypropan-2-ol: 3400 (OH); 1250 (Ar–O–C); in the C–F region: 1030, 1045, 1080, 1120, and 1180 cm.$^{-1}$.

1-Ethoxy-3-fluoroacetone: 1730 (C=O); 1025 and 1110 cm.$^{-1}$ (C–F and C–O–C).

1-Fluoro-3-phenoxyacetone: 1750 (C=O); 1240 (Ar–O–C); 1030, 1050, and 1120 cm.$^{-1}$ (C–F).

1-Fluoro-3-phenylpropan-2-ol: 3400 (OH), 1020 and 1100 broad with fine structure (C–F).

δ-Fluoromethyl-γ-valerolactone: 1790 (γ-lactone C=O), 1028, 1090, and 1120 (C–F).

1-Dimethylamino-3-fluoropropan-2-ol [3] has the hydroxyl peak at 3400 cm.$^{-1}$, shows a doublet at 2950 and 2800 cm.$^{-1}$ (hydrogen-bonded OH), and in the C–F region bands at 1015, 1040, and 1110 cm.$^{-1}$. In this region, the C–N frequency is also situated. The corresponding (2-acetoxy-3-fluoropropyl)trimethylammonium iodide shows bands at 1750 (ester C=O), and in the C–F region at 1030, 1050, 1080, and 1120 cm.$^{-1}$.

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670. *Organic Fluorine Compounds. Part XXI.* α-Fluorinated Keto-compounds.*

By Ernst D. Bergmann, Sasson Cohen, Eliahu Hoffman, and Zafrira Rand-Meir.

Alkyl or aryl fluoromethyl ketones are obtained from Grignard reagents and fluoroacetonitrile. 1,3-Difluoroacetone also reacts normally with phenylmagnesium bromide; fluoroacetone gives phenylacetone. Their Reformatzky reactions proceed normally.

Other reactions of these fluoro-ketones and fluorinated β-keto-esters have been studied, amongst them the reaction with keten.

For the preparation of fluoro- and difluoro-acetone, methods have been described [1,2] and were improved by Cherbuliez *et al.*[3] Direct replacement of chlorine by fluorine in α-chloro-ketones has been found possible also in the case of 2-chlorobutan-3-one, which gave a 55% yield of 3-fluorobutan-2-one. The ketals derived from α-chlorinated ketones did not exchange the chlorine for fluorine under the usual operating conditions, though bromoacetaldehyde diethyl acetal gave a 9% yield of fluoroacetaldehyde diethyl acetal.

In view of the somewhat abnormal behaviour of ethyl fluoroacetate [4] and fluoroacetone (see below), it is noteworthy that fluoroacetonitrile behaves normally towards Grignard reagents, giving alkyl or aryl fluoromethyl ketones in 25—80% yield. This seems the more surprising as aliphatic nitriles are often enolised by aliphatic organomagnesium compounds and do not yield ketones with them; [5] fluorine appears thus to depress the tendency to enolisation here as in other cases [6] (see below).

* Part XX, preceding paper.

[1] Kitano and Fukui, *Kogyo Kagaku Zasshi*, 1956, **59**, 395; *Chem. Abs.*, 1957, **51**, 11,282.
[2] Bergmann and Cohen, *J.*, 1958, 2259.
[3] Cherbuliez, de Picciotto, and Rabinowitz, *Helv. Chim. Acta*, 1960, **43**, 1143.
[4] Mirosevic-Sorgo and Saunders, *Tetrahedron*, 1959, **5**, 38.
[5] Bruylants, *Bull. Classe Sci., Acad. roy. Belg.*, 1922, **8**, 7; Mignonac and Hoffmann, *Compt. rend.*, 1930, **191**, 718.
[6] Blank, Mager, and Bergmann, *J.*, 1955, 2190.

Fuoroacetone and 1,3-difluoroacetone show to a large extent the normal reactivity of ketones, which appears to be only slightly modified by the fluorine atom. Similar observations have been recorded for more highly fluorinated ketones by Simmons and Wiley.[7]

Whilst 1,3-difluoroacetone, under defined conditions, reacts normally with phenylmagnesium bromide, giving 1,3-difluoro-2-phenylpropan-2-ol in 72% yield, fluoroacetone loses its fluorine under these conditions, and phenylacetone is obtained, probably by dehydrohalogenation and rearrangement of the primary product $CH_2F{\cdot}CPhMe{\cdot}OH$. Analogous reactions have been observed for chloroacetone [8] and ω-fluoroacetophenone.[9]

Condensation of fluoroacetone with ethyl cyanoacetate in the presence of ammonium acetate [10] yields, with spontaneous dehydration, ethyl α-cyano-γ-fluoro-β-methylcrotonate; on the other hand, attempts to dehydrate the hydroxy-esters obtained in the Reformatzky reaction of ethyl bromoacetate with fluoroacetone and 1,3-difluoroacetone gave no defined product, a behaviour which recalls that of other α-fluoro-hydroxy-compounds [11] and indicates that the C–OH bond in such compounds is strengthened. An attempt has also been made to condense the two ketones with ethyl chlorofluoroacetate,[12] as the latter compound has been shown to participate in this type of condensation:[13,14] the attempt failed, although acetone reacted smoothly with the chlorofluoro-ester (in the presence of magnesium), giving a 20% yield of ethyl α-fluoro-β-hydroxy-β-methylbutyrate which again could not be dehydrated without complete resinification. Another route to this ester is described in the following paper.

Condensation of 1,3-difluoroacetone with malonic acid in the presence of pyridine and piperidine gave a 40% yield of γ-fluoro-β-fluoromethyl-β-hydroxybutyric acid; in this case, also, the condensation was not accompanied by dehydration.[14a]

Fluoroacetone is attacked by elemental bromine preferentially at the methylene group, as proved by oxidation of the corresponding acid without loss of halogen. Greater reactivity of the methylene than of the methyl group in fluoroacetone is found also in reaction with formaldehyde which will be discussed later.

The influence of two fluorine atoms on the reactivity of the carbonyl group permits condensation of 1,3-difluoroacetone with dimethyl phosphite in the presence of sodium methoxide to give the ester $(CH_2F)_2C(OH){\cdot}PO(OMe)_2$; analogously, ethyl γγγ-trifluoroacetoacetate gives the phosphonate $EtO_2C{\cdot}CH_2{\cdot}C(CF_3)(OH){\cdot}PO(OMe)_2$.

For a more detailed study of fluorinated β-hydroxy-acids the reaction of various fluorinated keto-compounds with keten was studied, zinc chloride being used as catalyst. According to Hagemeyer,[15] the following general reaction was expected:

$$RR'C{=}O + CH_2{=}C{=}O \longrightarrow RR'C(O{-}CO){-}CH_2 \xrightarrow{R''OH} HO{\cdot}CRR'{\cdot}CH_2{\cdot}CO_2R''$$

However, from ethyl γ-fluoroacetoacetate and ethyl γγγ-trifluoroacetoacetate only the enol acetates could be isolated under these conditions, and ethyl acetoacetate itself gave the same result. On the other hand, ethyl α-fluoroacetoacetate gives the expected product

[7] Simmons and Wiley, *J. Amer. Chem. Soc.*, 1960, **82**, 2288.
[8] Tiffeneau, *Ann. Chim.* (*France*), 1913, **10**, 369.
[9] Bergmann and Kalmus, *J. Amer. Chem. Soc.*, 1954, **76**, 4137; cf. Ando, *Chem. Abs.*, 1960, **54**, 4492.
[10] Cope, Hofmann, Wyckoff, and Hardenbergh, *J. Amer. Chem. Soc.*, 1941, **63**, 3452; Whyte and Cope, *ibid.*, 1943, **65**, 1999; cf. Schnider and Hellerbach, *Helv. Chim. Acta*, 1950, **33**, 1437; Cragoe, Robb, and Sprague, *J. Org. Chem.*, 1950, **15**, 381.
[11] See, for literature, Bergmann, Moses, Neeman, Cohen, Kaluszyner, and Reuter, *J. Amer. Chem. Soc.*, 1957, **79**, 4174.
[12] Cf. McBee, Birmingham Symposium on Fluorine Chemistry, Butterworths, London, p. 44.
[13] Bergmann, Cohen, and Shahak, *J.*, 1959, 3278.
[14] McBee, Pierce, and Christman, *J. Amer. Chem. Soc.*, 1955, **77**, 1581.
[14a] Cf. Knunjants, Chen, and Gambaryan, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1960, 686.
[15] Hagemeyer, *Ind. Eng. Chem.*, 1949, **41**, 765; cf. Zaugg, "Organic Reactions," Wiley, New York, 1954, Vol. VIII, p. 305; cf. Knunjants and Cheburker, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1960, 678.

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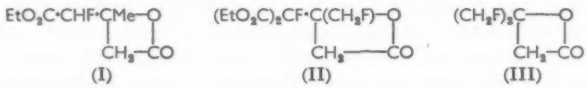
(I). It seems that the difference in behaviour of these compounds can be ascribed to the enolisation-depressing influence of α-fluorine and the enolisation-enhancing influence of γ-fluorine atoms. Enol titrations by Hieber's method [16] indeed led to the following values for the enol content of equilibrium mixtures: ethyl acetoacetate 7·7; ethyl α-fluoroacetoacetate 0·99; ethyl γ-fluoroacetoacetate 18·2; ethyl γγγ-trifluoroacetoacetate 49·0; diethyl malonate 0; diethyl fluoromalonate [17] 0·91%. In accordance with this explanation, a good yield of the β-lactone (II) was obtained from diethyl α-fluoro-α-fluoroacetylmalonate



$CH_2F{\cdot}CO{\cdot}CF(CO_2Et)_2$, which has no enolisable hydrogen atom, and from 1,3-difluoroacetone. The compound (III) formed in the latter case was converted by alcoholic potassium hydroxide solution into a mixture of the hydroxy-ester $(CH_2F)_2C(OH){\cdot}CH_2{\cdot}CO_2Et$ and the corresponding hydroxy-acid.

Experimental

The infrared data are for liquid films.

3-Fluorobutan-2-one.—In an efficient column, 3-chlorobutan-2-one [18] (106·5 g.) was added slowly at 170—180° to a mixture of potassium fluoride (87 g.), ethylene glycol (200 g.) and diethylene glycol (100 g.), so that the product distilled off continuously (70—120°). Fractionation gave *3-fluorobutan-2-one* (49 g., 55%), b. p. 74—76°, $\nu_{max.}$ 1725 (C=O), 1025 and 1100 (C–F) cm.$^{-1}$ (Found: C, 54·0; H, 7·9. C_4H_7FO requires C, 53·4; H, 7·8%), and some (8 g., 7%) starting material. The semicarbazone had m. p. 144°.

Fluoroacetaldehyde Diethyl Acetal.—Analogously, bromoacetaldehyde diethyl acetal (160 g.), potassium fluoride (80 g.), ethylene glycol (100 g.), and diethylene glycol (130 g.) gave a liquid, b. p. 120—140°, which was fractionated. The first fraction (20 g.), b. p. 78—80°, was mainly ethanol; the second (10 g., 9%), b. p. 120—122°, was the desired *acetal* (Found: C, 52·6; H, 9·4. $C_6H_{13}FO_2$ requires C, 52·9; H, 9·6%), $\nu_{max.}$ 1100—1180 (acetal [19]), 1013 (C–F) cm.$^{-1}$.

Reaction of Grignard Reagents with Fluoroacetonitrile.—To a Grignard solution from the alkyl or aryl bromide (0·20 mole) and magnesium (0·20 g.-atom) in ether (250 ml.) fluoroacetonitrile (0·20 mole) in ether (100 ml.) was added at −20° dropwise and with stirring, during 30—45 min. A pasty, ether-insoluble material was formed, so that vigorous mixing was required. After an additional hour's stirring at 0°, the mixture was poured on ice and sulphuric acid, the ethereal layer separated, and the aqueous phase extracted twice with ether. The combined ether extracts were dried (Na_2SO_4) and distilled. No attempt was made to find optimum conditions for the preparation of the ketones, but the following *fluoromethyl ketones* were obtained:

(1) *Butyl*, b. p. 55—56°/30 mm., n_D^{28} 1·4002 (34%) (Found: C, 61·2; H, 9·3; F, 16·0. $C_6H_{11}FO$ requires C, 61·0; H, 9·3; F, 16·1%).

(2) s-Butyl, b. p. 126—128°, n_D^{28} 1·4045 (34%) [2,4-*dinitrophenylhydrazone*, needles, m. p. 99—100° (from methanol) (Found: C, 48·8; H, 5·0; F, 6·3. $C_{12}H_{15}FN_4O_4$ requires C, 48·3; H, 5·0; F, 6·4%)].

(3) *Hexyl*, b. p. 55—60°/0·5 mm., n_D^{28} 1·4122 (24%) (Found: C, 65·7; H, 10·5. $C_8H_{15}FO$ requires C, 65·7; H, 10·3%) (no crystalline dinitrophenylhydrazone).

(4) Cyclopentyl, b. p. 73—74°/30 mm., n_D^{28} 1·4445 (32%) [2,4-*dinitrophenylhydrazone*, orange plates, m. p. 110—113° (from methanol) (Found: C, 52·0; H, 5·4; F, 6·3. $C_{13}H_{15}FN_4O_4$ requires C, 50·3; H, 5·0; F, 6·1%)].

(5) Cyclohexyl, b. p. 45—46°/0·6 mm., n_D^{26} 1·4510 (24%) [2,4-*dinitrophenylhydrazone*, prisms, m. p. 125—127° (from methanol) (Found: C, 52·0; H, 5·4; F, 6·3. $C_{14}H_{17}FN_4O_4$ requires C, 51·9; H, 5·3; F, 5·9%)].

(6) *Dodecyl*, b. p. 110—125°/0·6 mm., m. p. 34—35° [from light petroleum (b. p. 40—60°)]

[16] Hieber, *Ber.*, 1921, **54**, 902.
[17] Bergmann, Cohen, and Shahak, *J.*, 1959, 3286.
[18] Korschun, *Ber.*, 1905, **38**, 1125.
[19] Young and Tarrant, *J. Amer. Chem. Soc.*, 1948, **71**, 2432.

(54%) (Found: C, 73·1; H, 12·2; F, 8·1. $C_{14}H_{27}FO$ requires C, 73·0; H, 11·8; F, 8·3%) [2,4-*dinitrophenylhydrazone*, needles, m. p. 105—106° (from methanol) (Found: C, 58·8; H, 7·7; F, 4·7. $C_{20}H_{31}FN_4O_4$ requires C, 58·5; H, 7·6; F, 4·7%)].

(7) m-*Tolyl*, b. p. 85—90°/0·9 mm., n_D^{28} 1·5278 (80%) (Found: C, 71·2; H, 6·1; F, 12·2. C_9H_9FO requires C, 71·0; H, 5·9; F, 12·5%) [2,4-*dinitrophenylhydrazone*, orange prisms, m. p. 205—208° (from methanol) (Found: C, 54·3; H, 4·0; F, 6·1. $C_{15}H_{13}FN_4O_4$ requires C, 54·2; H, 3·9; F, 5·7%)].

(8) o-*Methoxyphenyl*, m. p. 88—89° (from methanol) (35%) (Found: C, 64·3; H, 5·7; F, 11·2. $C_9H_9FO_2$ requires C, 64·4; H, 5·4; F, 11·3%) [2,4-*dinitrophenylhydrazone*, dimorphic, orange prisms, m. p. 210—215° (Found: C, 51·5; H, 3·9; F, 5·6. $C_{15}H_{13}FN_4O_5$ requires C, 51·7; H, 3·7; F, 5·5%)].

These ketones had C=O maxima at (1—4) 1727, (5) 1681, (6) 1724, (7) 1700, (8) 1681 cm.$^{-1}$, and C–F absorption at (1) 1042, (2) 1020—1050, (3) 1053, (4) 1053, 1020, (5, 6) 1053, (7) 1031, (8) 1075, 1053, 1025 cm.$^{-1}$.

1,3-*Difluoro-2-phenylpropan-2-ol*.—At 0°, a solution of 1,3-difluoroacetone [2] (19 g.) in ether (50 ml.) was added to a Grignard solution prepared from magnesium (4·8 g.), bromobenzene (32 g.), and ether (100 ml.). After 15 min., the product was decomposed with ice-cold dilute sulphuric acid and the ethereal layer separated, dried, and distilled. The *alcohol* (25 g., 72%) boiled at 120—125°/24 mm., 82—83°/4 mm. (Found: C, 63·8; H, 5·8; F, 21·6. $C_9H_{10}F_2O$ requires C, 62·9; H, 5·8; F, 22·1%). $\lambda_{max.}$ (in EtOH) 250 mμ (log ε 3·00), $\nu_{max.}$ 3570, 3450, 1110, 1068, 1028, 1018 cm.$^{-1}$.

Reaction of Fluoroacetone with Phenylmagnesium Bromide.—At −10°, fluoroacetone [2] (7·6 g.) was added to a Grignard solution from magnesium (2·4 g.), bromobenzene (15·7 g.), and ether (100 ml.). The product was decomposed with ice and hydrochloric acid, and the ethereal layer washed with sodium hydrogen carbonate solution, dried, and distilled. The product (6·5 g., 48%) boiled at 114—116°/30 mm.; it was free from fluorine and the infrared spectrum showed a very pronounced carbonyl band at 1750 cm.$^{-1}$. By preparation of the 2,4-dinitrophenylhydrazone (m. p. 154°) and comparison with an authentic sample, the compound was identified as phenylacetone.

Ethyl α-Cyano-γ-fluoro-β-methylcrotonate.—A mixture of fluoroacetone (9 g.), ethyl cyanoacetate (11 g.), ammonium acetate (1·5 g.), acetic acid (5 g.), and benzene (30 ml.) was subjected to azeotropic distillation for 5 hr. The resulting solution was washed with water, dried, and distilled. The *ester* produced had b. p. 74—75°/1 mm. (7 g., 34%) (Found: C, 56·1; H, 6·3. $C_8H_{10}FNO_2$ requires C, 56·1; H, 5·9%).

Ethyl γ-Fluoro-β-hydroxy-β-methylbutyrate.—To a stirred mixture of zinc (7·8 g.) and benzene (60 ml.), fluoroacetone (9 g.) and ethyl bromoacetate (16·7 g.) in benzene (30 ml.) were added slowly at 50—60°. Heating was continued for 3 hr. and the mixture cooled and decomposed with ice and hydrochloric acid. Distillation of the benzene layer gave the desired *ester* (6 g., 40%), b. p. 90—95°/29 mm., 92°/25 mm., $\nu_{max.}$ 3500 (OH), 1750 (C=O), 1030 (C–F) cm.$^{-1}$ (Found: C, 51·6; H, 8·1; F, 11·3. $C_7H_{13}FO_3$ requires C, 51·2; H, 7·9; F, 11·6%).

Ethyl γ-Fluoro-β-fluoromethyl-β-hydroxybutyrate.—To a mixture of zinc (14·7 g.) and a little copper powder, a portion (20 ml.) of a solution of ethyl bromoacetate (38 g.) and 1,3-difluoroacetone (21 g.) in benzene (100 ml.) and toluene (50 ml.) was added, and the mixture was heated until the exothermic reaction set in. The rest of the solution was then added within 1 hr. without further heating and the product refluxed for 2 hr. and decomposed with ice and dilute sulphuric acid. The *ester* (15 g., 37%) boiled at 120—130°/40 mm. and, on redistillation, at 112°/30 mm., it had $\nu_{max.}$ 3480 (OH), 1725 (C=O), 1030 (C–F) cm.$^{-1}$ (Found: C, 46·0; H, 6·5; F, 21·4. $C_7H_{12}F_2O_3$ requires C, 46·1; H, 6·6; F, 20·9%).

Ethyl α-Fluoro-β-hydroxy-β-methylbutyrate.—To a suspension of magnesium (8·5 g.), activated with a little iodine, in benzene (30 ml.), a mixture of acetone (17·5 g.), ethyl chlorofluoroacetate [19] (35 g.), and benzene (70 ml.) was added so that the whole boiled gently. The mixture was refluxed for 30 min. more and then decomposed with ice-cold dilute sulphuric acid. Distillation gave the *hydroxy-ester* (8 g., 20%), b. p. 90°/20 mm., that slowly decomposed (Found: C, 50·8; H, 8·3; F, 11·9; OEt, 28·5. $C_7H_{13}FO_3$ requires C, 51·2; H, 7·9; F, 11·6; OEt, 27·4%) and had $\nu_{max.}$ 3230 (hydrogen-bonded OH), 1130 (broad, C–F) cm.$^{-1}$.

γ-Fluoro-β-fluoromethyl-β-hydroxybutyric Acid.—A mixture of 1,3-difluoroacetone (23 g.), malonic acid (25 g.), pyridine (40 g.), and piperidine (1 ml.) was kept at room temperature for 24 hr. and the excess of pyridine then removed *in vacuo*. 63% Hydrobromic acid (30 ml.) was

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added to the residue and the solution again brought to dryness *in vacuo*. Distillation *in vacuo* gave a viscous liquid which was dissolved in acetone, filtered (from a little pyridine hydrobromide), and distilled again. The *acid* (15 g., 40%) had b. p. 120—125°/0·5 mm., $\nu_{max.}$ 3420 (OH, broad), 1724 (C=O), 1030 (C–F) cm.$^{-1}$ (Found: C, 38·5; H, 5·0. $C_5H_5F_2O_2$ requires C, 38·9; H, 5·2%).

Bromination of Fluoroacetone.—Bromine (80 g.) was added slowly to fluoroacetone (38 g.) in chloroform (150 ml.). After the first drops had been added, the solution had to be heated slightly, until the reaction set in. The remainder was added at 10—20°. The time required was 90 min. The solution was washed with sodium hydrogen carbonate solution and dried. Distillation gave fractions, b. p. 80—110° (60 g.) and 65—85°/17 mm. (25 g.). The first fraction, on redistillation, boiled at 106—110° (35 g., 45%) and was 1-*bromo*-1-*fluoroacetone* (Found: C, 23·4; H, 2·6. C_3H_4BrFO requires C, 23·2; H, 2·6%); it had $\nu_{max.}$ 1740 (C=O), 1180, 1120, 1080, and 1030, (C–F), 665 (C–Br) cm.$^{-1}$. The compound (35 g.) was added to 80% nitric acid (112 ml.) with stirring. When the exothermic reaction subsided, the mixture was heated at 100° for 2 hr. Distillation gave 16 g. (45%) of fluorobromoacetic acid, b. p. 98—99°/29 mm., n_D^{25} 1·4382 (Found: C, 15·3; H, 1·6; Br, 50·3. Calc. for $C_2H_2BrFO_2$: C, 15·3; H, 1·3; Br, 51·0%).

The second fraction boiled, on redistillation, at 82—83°/17 mm. (22 g., 19%) and was a crude dibromofluoroacetone (Found: C, 16·4; H, 1·6; F, 8·6. $C_3H_3Br_2FO$ requires C, 15·4; H, 1·3; F, 8·1%).

Dimethyl 2-Fluoro-1-fluoromethyl-1-hydroxyethylphosphonate.—To a mixture of dimethyl phosphite (40 g.) and 2N-methanolic sodium methoxide (50 ml.), 1,3-difluoroacetone (28·2 g.) was added. After 16 hr., glacial acetic acid (6 g.) was added and the product distilled. The *ester* (13 g., 21%) had b. p. 125—127°/4 mm. (Found: C, 29·1; H, 5·3. $C_5H_{11}PF_2O_4$ requires C, 29·4; H, 5·4%). $\nu_{max.}$ 3480 (OH), 1750 (C=O), 1240 (P=O),[20] 1080 (C–F), 1018 (C–F) cm.$^{-1}$.

Dimethyl 2-Ethoxycarbonyl-1-hydroxy-1-trifluoromethylethylphosphonate.—A mixture of dimethyl phosphite (11 g.) and ethyl γγγ-trifluoroacetoacetate [21] (18·1 g.) was refluxed, and 2N-sodium methoxide (5 ml.) added. The mixture was heated for 1 hr. more at 100° and distilled. The *product* (10 g., 30%) boiled at 116—118°/3 mm. (Found: C, 32·9; H, 5·1. $C_8H_{14}PF_3O_6$ requires C, 32·7; H, 4·8%).

γ-Fluoro-β-fluoromethyl-β-butyrolactone (III).—Keten [22] (~1·5 mol.) was passed into a stirred solution of 1,3-difluoroacetone (40 g.) and freshly fused zinc chloride (1 g.) in anhydrous ether (50 ml.) at 25—30°; then a saturated solution of sodium carbonate (2 g.) in water was added, and the mixture stirred for another hour. The solution was then filtered and distilled. The *lactone* (49 g., 95%) had b. p. 105—107°/16 mm., n_D^{13} 1·4140 $\nu_{max.}$ 1850 (β-lactone), 1030 (C–F) cm.$^{-1}$ (Found: C, 44·5; H, 4·3. $C_5H_6F_2O_2$ requires C, 44·2; H, 4·4%).

Potassium hydroxide (6 g.) in ethanol (20 ml.) was added at 0° to a solution of this lactone (14 g.) in ethanol (50 ml.), and the mixture was left overnight at room temperature; aqueous concentrated hydrochloric acid was then added until the reaction was acid; the solution was filtered and distilled, giving *ethyl γ-fluoro-β-fluoromethyl-β-hydroxybutyrate* (6 g., 32%), b. p. 53—54°/0·8 mm. (Found: C, 46·7; H, 6·7; F, 21·0. $C_7H_{12}F_2O_3$ requires C, 46·2; H, 6·6; F, 20·9%), and *γ-fluoro-β-fluoromethyl-β-hydroxybutyric acid* (6 g., 38%), b. p. 113—115°/0·6 mm. (Found: C, 40·1; H, 5·4; F, 24·4. $C_5H_8F_2O_3$ requires C, 38·9; H, 5·2; F, 24·6%).

Enol Acetate of Ethyl γγγ-Trifluoroacetoacetate.—Keten was passed into a solution of ethyl γγγ-trifluoroacetoacetate [22] (12 g.) and zinc chloride (0·5 g.) in anhydrous ether (50 ml.), as described above. The catalyst was destroyed with sodium carbonate (1 g.) in a little water, and the filtered solution was distilled. The *enol acetate* (10 g., 68%) had b. p. 72—74°/15 mm., n_D^{13} 1·3940, $\nu_{max.}$ 1810 (enol acetate [23]), 1730 (unsaturated ester C=O), 1075 and 1030 (C–F) cm.$^{-1}$ (Found: C, 42·1; H, 4·2. $C_8H_9F_3O_4$ requires C, 42·5; H, 4·0%).

Ethyl β-Acetoxycrotonate.—Keten was passed into a stirred mixture of ethyl acetoacetate (86 g.) and zinc chloride (2 g.) at 30—33°. Working up as above gave *ethyl β-acetoxycrotonate* (48 g., 42%), b. p. 105—107°/20 mm. (lit.,[24] 99°/12 mm.), n_D^{13} 1·4510 (Found: C, 56·3; H, 6·8. Calc. for $C_8H_{12}O_4$: C, 55·8; H, 6·9%).

[20] Bellamy and Beecher, *J.*, 1952, 475.
[21] McBee, Pierce, Kilbourne, and Wilson, *J. Amer. Chem. Soc.*, 1953, **75**, 3152.
[22] Hanford and Sauer, "Organic Reactions," Wiley, New York, 1946, Vol. III, p. 108.
[23] The frequency is higher than usual (1750—1770 cm.$^{-1}$; see, *e.g.*, Jones and Herling, *J. Org. Chem.*, 1954, **19**, 1252) probably because of the influence of the three neighbouring fluorine atoms.
[24] Michael, *Ber.*, 1905, **38**, 2083.

γγ-Diethoxycarbonyl-γ-fluoro-β-fluoromethyl-β-butyrolactone (II).—Keten was passed into a stirred solution of diethyl α-fluoro-α-fluoroacetylmalonate [17] (18 g.) and zinc chloride (1 g.) in anhydrous ether (50 ml.). The catalyst was destroyed as described above. Fractionation gave some starting material, then the β-lactone (II) (5 g., 24%), b. p. 149—150°/0·5 mm., $\nu_{max.}$ 1870 (β-lactone), 1770 (α-halogenated ester C=O [25]), and in the C–F region 1120, 1060, 1025 cm.$^{-1}$ (Found: C, 48·1; H, 5·6. $C_{11}H_{14}F_2O_6$ requires C, 47·2; H, 5·0%).

γ-Ethoxycarbonyl-γ-fluoro-β-methyl-β-butyrolactone (I).—Keten was passed into a solution of ethyl α-fluoroacetoacetate [13] (14 g.) and zinc chloride (0·5 g.) in chloroform (50 ml.) at 5—10°. A saturated solution of sodium carbonate (5 ml.) was then added, and the mixture was stirred for 1 hr. The chloroform solution was separated, filtered, and distilled. The *β-lactone* (8 g., 45%) had b. p. 108—110°/0·2 mm. (polymerised on prolonged heating), $\nu_{max.}$ 1850 (β-lactone), 1740 (α-halogenated ester C=O [25]), 1090 and 1025 (C–F) cm.$^{-1}$ (Found: C, 50·2; H, 6·0; F, 9·5. $C_8H_{11}FO_4$ requires C, 50·5; H, 5·8; F, 10·0%).

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[25] Cf. Gillette, *J. Amer. Chem. Soc.*, 1936, **58**, 1143.

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671. *Organic Fluorine Compounds. Part XXII.* Fluorine Analogues of Mevalonic Acid.*

By Ernst D. Bergmann and Sasson Cohen.

γ-Fluoromevalonolactone has been synthetised, the essential step being condensation of fluoroacetone with formaldehyde at the methylene group; it powerfully inhibits the incorporation of acetate or mevalonate.

A synthesis of α-fluoromevalonolactone, based on the condensation of ethyl sodiofluoroacetate with 4-hydroxybutan-2-one or its acetate, gave only impure material owing to the ready dehydration.

The biosynthetic importance of mevalonic acid and the ability of fluorine to convert a metabolite into an antimetabolite made it interesting to study fluoromevalonolactones. Of the three structural isomers, (I) has been recently described [1] and studied.[2] The present paper describes some additional attempts at the oxidation of the intermediate (VII) and related reactions, but in the main it deals with the γ- (II) and the α-isomer (III). For the synthesis of (I) by application of the method of Folker *et al.*,[3] it was necessary to prepare 1-fluoro-4-hydroxybutan-2-one. The diethyl or ethylene ketal of the easily available [4] ethyl γ-fluoroacetoacetate (IV) was reduced with lithium aluminium hydride, but the product was very unstable and did not lend itself to further reaction. Since condensation of the ester (IV) with keten leads only to the corresponding enol acetate,[5] preparation of the acid (V) by oxidation of 4-fluoromethylhepta-1,6-dien-4-ol (VII) and its reduction to (VI) was attempted, but without success. Also, the acetate of this alcohol, obtained in 42% yield from ethyl fluoroacetate and allylmagnesium bromide, was unusually resistant to chromic acid in 80% acetic acid: the only product isolated contained two oxygen atoms more than the starting material and may have been the diepoxide.[5a]

* Part XXI, preceding paper.

[1] Tschesche and Machleidt, *Annalen*, 1960, **631**, 61.
[2] Singer, Januszka, and Berman, *Proc. Soc. Exp. Biol. Med.*, 1959, **102**, 170.
[3] Hoffman *et al.*, *J. Amer. Chem. Soc.*, 1957, **79**, 2316.
[4] Bergmann, Cohen, and Shahak, *J.*, 1959, 3278.
[5] Bergmann, Cohen, Hoffman, and Meir-Rand, preceding paper.
[5a] Cf. Sankyo Co. Ltd., Jap. Pat. 3876; *Chem. Abs.*, 1961, **55**, 1452.

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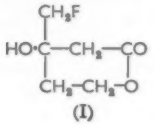
For the synthesis of compound (II), fluoroacetone was condensed with formaldehyde in the presence of sodium methoxide. In analogy to the behaviour of chloroacetone,[6] and in view of the stability of the product, it was probably 3-fluoro-4-hydroxybutan-2-one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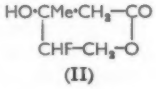
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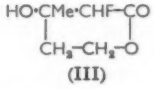
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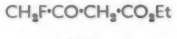
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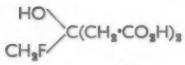
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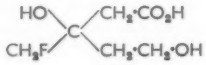
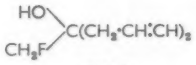
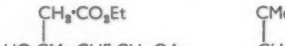
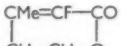

(VI)

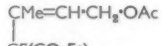

(VII)

(VIII), and this was proved by a positive iodoform test. The derived acetate with zinc and ethyl bromoacetate gave ethyl 8-acetoxy-γ-fluoro-β-hydroxy-β-methylvalerate (IX), which was smoothly converted by alkali into the stable γ-fluoromevalonolactone (II). This product is liquid and appears to be sterically homogeneous; however, this point has not been established beyond doubt.

(VIII)


(IX)


(X)


(XI)

It was expected that 3-oxobutyl acetate would react normally with ethyl chlorofluoroacetate in the same way as acetone [5] and ethyl methyl ketone.[7] However, with zinc or magnesium, either no reaction took place or untractable resins were obtained. Recourse was, therefore, had to the reaction [7] between the sodium derivative of the ethyl fluoroacetate and 4-hydroxybutan-2-one or its acetate. The infrared spectrum of the crude product corresponded to formula (III) which could have been formed directly in this reaction; however, upon distillation, water was split off and, after repeated distillation, the pure unsaturated lactone (X) was obtained. In the Reformatzky reaction between 3-oxobutyl acetate and diethyl bromofluoromalonate a product was formed which gave correct analyses for the unsaturated ester (XI). A boiling mixture of glacial acetic and hydrochloric acids cyclised this to the unsaturated lactone (X).

Dr. F. M. Singer [8] of the Squibb Institute, New Brunswick, N.J., has kindly compared the influence of the lactones (I) and (II) on the conversion of acetate and mevalonate, respectively, into cholesterol. The lactone (II) has a very strong inhibitory effect in both systems; in the acetate system, it is practically as active as lactone (I) (96% compared with 99% of inhibition), but in the mevalonate system less so (61%, compared with 88%).

A preliminary report on the synthetic experiments has been published.[8]

Experimental

Infrared data refer to liquid films.

3-Fluoro-4-hydroxybutan-2-one (VIII).—A stirred mixture of fluoroacetone (170 g.), paraformaldehyde (30 g.), and 2M-methanolic sodium methoxide (4 ml.) was heated on a water-bath for 5 min. Glacial acetic acid (1 ml.) was added, and the excess of fluoroacetone removed at 20 mm. and collected in a carbon dioxide–acetone trap. The recovered ketone was again treated as described above, the operation being carried out three times, in all. The product from these operations was combined and distilled, to yield the *hydroxy-ketone* (65 g., 42%), b. p.

[6] Buchman and Sargent, *J. Amer. Chem. Soc.*, 1945, **67**, 400; cf. the study by Bnkowska (*Roczniki Chem.*, 1958, **32**, 739; *Chem. Abs.*, 1959, **53**, 4117) of the preferred direction of the enolisation of chloroacetone.

[7] Bergmann and Cohen, *J.*, 1961, 3537.

[8] Bergmann and Cohen, *Tetrahedron Letters*, 1960, No. 8, 20.

57—58° (0·5 mm.), $\nu_{max.}$ 1724 (C=O, halogen-substituted [9]), 1100 and 1064 (C–F) cm.$^{-1}$ (Found: C, 45·8; H, 6·5; F, 18·2. $C_6H_7FO_2$ requires C, 45·3; H, 6·6; F, 17·9%).

The product (53 g.) was added, dropwise and with stirring, to acetic anhydride (60 g.) containing 5 drops of the boron trifluoride–ether complex at 30—35°. The mixture was stirred for 2 hr. at this temperature; then 2M-methanolic sodium methoxide (2 ml.) was added, and the mixture fractionated. The *acetate* (50 g., 68%) had b. p. 54—55°/0·4 mm., $\nu_{max.}$ 1724 (C=O), and (C–F) 1020, 1050, 1110 cm.$^{-1}$ (Found: C, 48·7; H, 6·3. $C_6H_9FO_3$ requires C, 48·6; H, 6·1%).

Ethyl δ-Acetoxy-γ-fluoro-β-methyl-β-hydroxyvalerate (IX).—A solution of the foregoing compound (50 g.) and ethyl bromoacetate (68 g.) in ether (350 ml.) was added, dropwise and with stirring, to activated zinc foil (26·5 g.) and the mixture refluxed until the zinc had reacted. After decomposition with sulphuric acid and crushed ice, separation of the ethereal layer, drying, and distillation gave the *ester* (45 g., 59%), b. p. 124—125°/0·4 mm., $\nu_{max.}$ 3400 (OH), 1740 (ester C=O), 1020, 1060, and 1090 (C–F) cm.$^{-1}$ (Found: C, 51·0; H, 7·4; F, 8·4. $C_{10}H_{17}FO_5$ requires C, 50·9; H, 7·2; F, 8·1%).

γ-Fluoromevalonolactone (II).—The foregoing ester (11·2 g.) in methanol (50 ml.) was treated at 0° with potassium hydroxide (5·6 g.) in methanol (30 ml.), then left at room temperature for 24 hr. Acetic acid was added to pH 5, and the mixture diluted with water (100 ml.) and extracted three times with ether. The aqueous phase was acidified with hydrochloric acid to pH 2—3 and extracted with ethyl acetate (3 × 50 ml.). The extracts were treated with charcoal and sodium sulphate, filtered, and distilled, to yield *γ-fluoromevalonolactone* (2 g., 27%), b. p. 124—125°/0·4 mm. (Found: C, 49·2; H, 6·3; F, 13·4. $C_6H_9FO_3$ requires C, 48·6; H, 6·1; F, 12·9%). The infrared spectrum showed the hydroxyl band at 3400 cm.$^{-1}$, in the C–F region bands at 1010, 1070, and 1100 cm.$^{-1}$, and the carbonyl band at 1720 cm.$^{-1}$ (somewhat low for a six-membered ring lactone).

α-Fluoromevalonolactone (III) *and 2-Fluoro-5-hydroxy-3-methylpent-2-enoic Acid Lactone* (X).—(*a*) Ethyl fluoroacetate (35 g.) in dry ether (100 ml.) was added to a stirred suspension of sodium hydride (8 g.) in dry ether (50 ml.) at 0—5° (the reaction was initiated by the addition of a few drops of ethanol). The mixture was stirred for 2 hr. at this temperature, then a solution of 3-oxobutyl acetate [3] (36 g.) in ether (50 ml.) was added dropwise, and the stirring continued for 3 hr. After decomposition with sulphuric acid and ice, separation of the organic material, and distillation, a mixture (9 g.) of α-fluoromevalonolactone (III) and its unsaturated analogue (X) was obtained. The infrared spectrum indicated the presence of a hydroxyl (3500 cm.$^{-1}$) and a C=O group (1625 cm.$^{-1}$); in the fluorine region, three frequencies were observed (1030, 1050, and 1100 cm.$^{-1}$). The carbonyl band was broad (centre at 1748 cm.$^{-1}$); it possibly represents the absorption both of the α-fluorinated saturated lactone-carbonyl, expected at 1745, and of the α-fluorinated αβ-unsaturated carbonyl, at 1754 cm.$^{-1}$ (see below).

On repeated distillation, the unsaturated *lactone* (X), b. p. 150—160°/0·5 mm., was obtained pure (Found: C, 55·8; H, 5·6; F, 14·3. $C_6H_7FO_2$ requires C, 55·4; H, 5·4; F, 14·6%), $\nu_{max.}$ 1660 and 1754 (C=O), 1025 and 1075 (C–F) cm.$^{-1}$.

(*b*) Ethyl fluoroacetate (106 g.) was added dropwise to a stirred suspension of sodium hydride (12 g.) in tetrahydrofuran [10] (300 ml.) at 0°. Stirring was continued until a clear brown solution had been formed; 3-oxobutyl acetate (51 g.) was then added dropwise, and the solution stirred for 4 hr., poured into an excess of ice-cold sulphuric acid, and extracted with ether. The ethereal extract was dried (Na_2SO_4) and distilled, to yield ethyl αγ-difluoroacetoacetate and a mixture (8 g.), b. p. 100—160°/0·5 mm. On redistillation, the product boiled at 120—125°/0·2 mm. and had n_D^{19} 1·4646 (Found: C, 51·2; H, 5·8; F, 13·7%).

(*c*) To the enol derivative of ethyl fluoroacetate (106 g.), prepared with sodium hydride (12 g.) in tetrahydrofuran (300 ml.), 4-hydroxybutan-2-one (44 g.) was added dropwise and with stirring at 0°. The solution was stirred at this temperature for 4 hr., left overnight, and worked up as above. Distillation gave material (15 g., 20%) boiling at 100—150°/0·5 mm. with much decomposition, and on redistillation gave material (10 g., 13·5%), b. p. 120—125°/0·2 mm., n_D^{19} 1·4623 (Found: C, 52·1; H, 6·1%).

Diethyl Bromofluoromalonate.—A stirred solution of diethyl fluoromalonate [11] (46 g.) in carbon tetrachloride (50 c.c.) was irradiated with ultraviolet light, while bromine (43 g.) was

[9] Cherrier, *Compt. rend.*, 1947, **225**, 997.
[10] Cf. Lawesson and Busch, *Acta Chem. Scand.*, 1959, **13**, 1717.
[11] Bergmann, Cohen, and Shahak, *J.*, 1959, 3286.

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added dropwise. The reaction was very sluggish and required intermittent refluxing. When most of the bromine had reacted, the solution was cooled, washed with 5% sodium carbonate solution and water, dried (Na_2SO_4), and distilled. *Diethyl bromofluoromalonate* (43·5 g., 63%) boiled at 126—128°/27 mm. and had $\nu_{max.}$ 1763 (C=O, raised by halogen substitution [12]), 1045 and 1025 (C–F) cm.$^{-1}$ (Found: C, 32·8; H, 4·1. $C_7H_{10}BrFO_4$ requires C, 32·7; H, 3·9%).

Diethyl 4-Acetoxy-1-fluoro-2-methylbut-2-ene-1,1-dicarboxylate (XI).—A solution of diethyl bromofluoromalonate (35 g.) and 3-oxobutyl acetate (18 g.) in anhydrous ether (100 ml.) was added, dropwise and with stirring, to clean zinc foil (10 g.). The mixture was refluxed for 5 hr., then poured on ice and an excess of sulphuric acid; the ethereal solution was separated, dried, and distilled. The fraction of b. p. 100—150°/0·5 mm. (15 g., 37%) was redistilled, to yield the *ester* (XI), b. p. 120—121°/0·5 mm., $\nu_{max.}$ 1754 (C=O, raised by halogen substitution [12]), shoulder at 1725 (ester C=O), 1690 (C=O double bond), 1100 and 1030 (C–F) cm.$^{-1}$ (Found: C, 53·2; H, 6·7. $C_{13}H_{19}FO_6$ requires C, 53·7; H, 6·6%).

2-Fluoro-5-hydroxy-3-methylpent-2-enoic Acid Lactone (X).—The foregoing compound (5 g.) was heated on a water-bath with acetic acid (10 ml.) and hydrochloric acid (10 ml.) for 30 min. Distillation gave the unsaturated lactone (X), b. p. 150—160°/0·5 mm. (Found: C, 54·5; H, 5·8. Calc. for $C_6H_7FO_2$: C, 55·4; H, 5·4%). The infrared spectrum was identical with that of the compound prepared by the alternative method.

4-Fluoromethylhepta-1,6-dien-4-ol (VII).—To a Grignard solution [from magnesium (24 g.) and allyl bromide (60·5 g.) in ether (300 ml.)], ethyl fluoroacetate (26·5 g.) in ether (100 ml.) was added dropwise and with stirring at −20°. Vigorous stirring was maintained at this temperature for 2 hr., then the mixture was poured on ice and sulphuric acid. The ethereal solution was separated, dried (Na_2SO_4), and distilled. The alcohol (15 g., 42%) had b. p. 72—73°/20 mm., (lit.,[1] 59°/12 mm.), $\nu_{max.}$ 3420 (OH), 1650 (C=C), 1010 (C–F) cm.$^{-1}$ (Found: C, 67·1; H, 9·1; F, 12·6. $C_8H_{13}FO$ requires C, 66·7; H, 9·0; F, 13·2%).

The boron trifluoride–ether complex (3 drops) was added cautiously to a mixture of the alcohol (14 g.) and acetic anhydride (12 g.). When the reaction subsided, the mixture was heated on a water-bath for 1 hr. and distilled. The *acetate* (16 g., 85%) boiled at 86—87°/20 mm. and had $\nu_{max.}$ 1740 (C=O), 1650 (C=C), 1020 (C–F) cm.$^{-1}$ (Found: C, 64·6; H, 8·2; F, 10·0. $C_{10}H_{15}FO_2$ requires C, 64·5; H, 8·1; F, 10·2%).

4-Acetoxy-1,2:6,7-diepoxy-4-fluoromethylheptane (?).—The preceding compound (14 g.) was dissolved in acetic acid (80 ml.) and water (20 ml.), and chromic anhydride (25 g.) added in small portions and with stirring at 20—25°. The mixture was stirred for 12 hr. at room temperature, diluted with water, and extracted repeatedly with ether. Distillation of the extract gave unchanged acetate (3 g.) and the (?) diepoxide (2 g.), b. p. 114—116°/0·5 mm., which was insoluble in water, soluble in all organic solvents. $\nu_{max.}$ 1728 (C=O), 1030 (C–F), 1250 and 930 (epoxide [13]) cm.$^{-1}$ (Found: C, 54·2; H, 6·5. Calc. for $C_{10}H_{13}FO_4$: C, 55·0; H, 6·9%).

Ethyl ββ-Diethoxy-γ-fluorobutyrate.—A mixture of ethyl γ-fluoroacetoacetate [4] (71 g.), ethyl orthoformate (142 g.), and boron trifluoride–ether complex (2 ml.) was kept for 48 hr. at room temperature, potassium hydroxide (4 g.) in a little methanol added, and the mixture fractionated. The *ketal* produced (70 g., 66%) boiled at 63—65°/0·5 mm. (Found: C, 54·2; H, 8·6. $C_{10}H_{19}FO_4$ requires C, 54·1; H, 8·6%).

Ethyl (2-Fluoromethyl-1,3-dioxolan-2-yl)acetate.—Ethyl γ-fluoroacetoacetate (10 g.) was azeotropically distilled with ethylene glycol (4 g.), benzene (50 ml.), and a trace of toluene-*p*-sulphonic acid. Then solid calcium carbonate was added and the filtered solution distilled. The *ketal* boiled at 104—106°/18 mm. (Found: C, 49·7; H, 6·7; F, 10·4. $C_8H_{13}FO_4$ requires C, 50·0; H, 6·7; F, 10·0%).

Ethyl α-fluoro-α-(2-methyl-1,3-dioxolan-2-yl)acetate, prepared analogously, had b. p. 100—101°/18 mm. (Found: C, 50·0; H, 6·9; F, 10·0%).

Part of this work was carried out by one of us (E. D. B.) at the Biochemistry Department, College of Physicians and Surgeons, Columbia University, New York, during the tenure of a guest professorship. We thank Dr. David Rittenberg, Head of the Department, for his hospitality and advice.

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[*Received, January 5th*, 1961.]

[12] Cf. Hartwell, Richards, and Thompson, *J.*, 1948, 1436.
[13] Bergmann, Yaroslavsky, and Weiler-Feilchenfeld, *J. Amer. Chem. Soc.*, 1959, **81**, 2775.

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672. Anogeissus schimperi *Gum.*

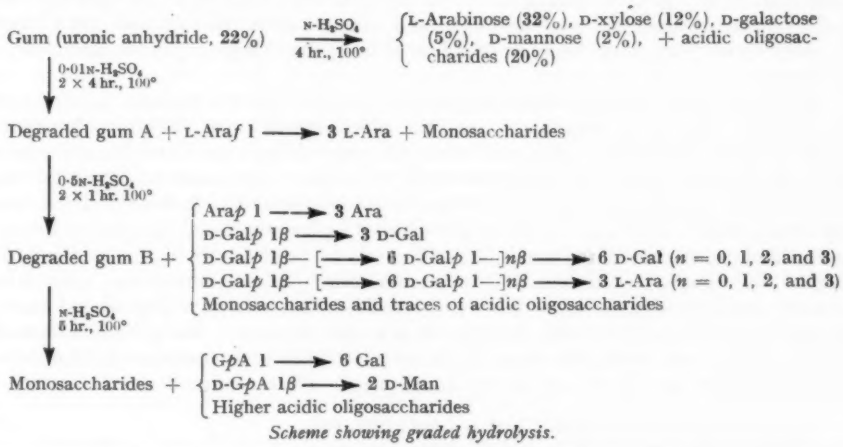
By G. O. Aspinall and T. B. Christensen.

Anogeissus schimperi gum contains residues of L-arabinose, D-xylose, D-galactose, D-mannose, and D-glucuronic acid. Controlled acid hydrolysis of the gum removes some of the arabinose residues preferentially, and 3-*O*-L-arabinofuranosyl-L-arabinose has been isolated during the early stages of the hydrolysis. Further graded hydrolysis afforded complex mixtures of neutral and acidic oligosaccharides amongst which the following have been characterised: 3-*O*-β-D-galactopyranosyl-D-gaclatose, the first four members of the series *O*-β-D-galactopyranosyl-[(1 ⟶ 6)-*O*-β-D-galactopyranosyl]$_n$-(1 ⟶ 3)-L-arabinose (n = 0—3), and 2-*O*-(β-D-glucopyranosyluronic acid)-D-mannose. The recognised structural features of the gum are compared with those of gum ghatti.

The gum exudate from *Anogeissus schimperi*, or marike gum, is isolated from a tree found in Northern Nigeria and the eastern parts of the Sudan. McIlroy [1] showed the presence in it of arabinose, galactose, and glucuronic acid residues. A quantity of the gum was kindly placed at our disposal by Professor R. J. McIlroy and some of the structural features of the gum have been investigated by an examination of its partial acid hydrolysis.

A preliminary investigation (with Dr. Barbara J. Auret and Mr. H. Wilkie) showed the gum to contain ~22% of uronic anhydride, and to give on hydrolysis, D-xylose (12%), L-arabinose (32%), D-galactose (5%), D-mannose (2%), traces of rhamnose, ribose, and fucose, and a mixture of acidic oligosaccharides (20%), which was shown by paper chromatography to contain a main component indistinguishable from 2-*O*-(β-D-glucopyranosyluronic acid)-D-mannose. In view of the low recovery of sugars in this experiment, the quoted proportions of sugars are minimum values, and it is probable that those of acidic oligosaccharides and hexose sugars are relatively lower than those of pentose sugars.

In preliminary experiments on the partial acid hydrolysis of the gum under varying conditions many different oligosaccharides, both neutral and acidic, were detected as products. Accordingly, graded acid hydrolysis was carried out in three stages (see flow sheet), degraded gums A and B being separated from the soluble sugars after the first and


Gum (uronic anhydride, 22%)
N-H2SO4
4 hr., 100°
L-Arabinose (32%), D-xylose (12%), D-galactose (5%), D-mannose (2%), + acidic oligosaccharides (20%)
0·01N-H2SO4
2 × 4 hr., 100°
Degraded gum A + L-Arafl ⟶ 3 L-Ara + Monosaccharides
0·5N-H2SO4
2 × 1 hr. 100°
Degraded gum B +
Arap 1 ⟶ 3 Ara
D-Galp 1β ⟶ 3 D-Gal
D-Galp 1β— [⟶ 6 D-Galp 1—]nβ ⟶ 6 D-Gal (n = 0, 1, 2, and 3)
D-Galp 1β— [⟶ 6 D-Galp 1—]nβ ⟶ 3 L-Ara (n = 0, 1, 2, and 3)
Monosaccharides and traces of acidic oligosaccharides
N-H2SO4
5 hr., 100°
Monosaccharides +
GpA 1 ⟶ 6 Gal
D-GpA 1β ⟶ 2 D-Man
Higher acidic oligosaccharides

Scheme showing graded hydrolysis.

[1] McIlroy, *J.*, 1952, 1918.

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the second stage. At each stage the various oligosaccharides were fractionated by adsorption and/or partition chromatography.

Mild acid hydrolysis resulted in cleavage of most of the arabinose and xylose residues, leaving degraded gum A with a relatively resistant core, composed largely of galactose, mannose, and glucuronic acid residues. The main disaccharide, isolated at this stage, appeared to be chromatographically and ionophoretically homogeneous and gave only arabinose on hydrolysis. Methylation and then hydrolysis of this disaccharide gave 2,3,5-tri- and 2,4-di-*O*-methyl-L-arabinose as the principal products, with smaller amounts of 2,3,4-tri-, and 2,5- and 3,4-di-*O*-methylarabinose. It follows that the fraction was composed largely of 3-*O*-L-arabinofuranosyl-L-arabinose, which was contaminated with other arabinose-containing oligosaccharides. The optical rotation ($[\alpha]_D$ +107°) of the fraction was rather higher than those reported for 3-*O*-L-arabinofuranosyl-L-arabinose isolated from sugar-beet araban [2] and *Acacia pycnantha* gum,[3] again suggesting contamination with other sugars. Other fractions were shown by chromatography of the sugars and their hydrolysis products to contain three oligosaccharides composed solely of arabinose residues (one of them indistinguishable from 3-*O*-β-L-arabinopyranosyl-L-arabinose), 3-*O*-β-galactopyranosylarabinose, and a disaccharide containing mannose and xylose residues.

The second stage of the partial hydrolysis gave mainly neutral oligosaccharides, including the following crystalline sugars which were identified by comparison with authentic specimens: 3-*O*-β-D-galactopyranosyl-D-galactose; and the first four members of the series, *O*-β-D-galactopyranosyl-[(1 → 6)-*O*-β-D-galactopyranosyl]$_n$-(1 → 3)-L-arabinose (n = 0—3), which have been previously characterised as partial hydrolysis products of gum ghatti.[4] The four members of this polymer-homologous series were only identified by the chromatographic mobilities of the sugars and their partial hydrolysis products, but there can be little doubt as to their identity in view of the isolation of the crystalline polygalactosylarabinose oligosaccharides. An arabinobiose was chromatographically and ionophoretically indistinguishable from 3-*O*-β-L-arabinopyranosyl-L-arabinose, and hydrolysis of the methylated derivative gave 2,3,4-tri- and 2,4-di-*O*-methylarabinose. In addition, small amounts of three acidic oligosaccharides were found at this stage, two of them being chromatographically indistinguishable from 2-*O*-(β-D-glucopyranosyluronic acid)-D-mannose and 6-*O*-(β-D-glucopyranosyluronic acid)-D-galactose; the third acidic sugar was a trisaccharide, *O*-(glucosyluronic acid)-(1 → 6)-*O*-galactosylarabinose, since hydrolysis of the glycitol (obtained by borohydride reduction) gave 6-*O*-(glucosyluronic acid)galactose, galactose, and arabitol, and reduction of the methyl ester methyl glycosides with potassium borohydride followed by hydrolysis gave glucose, galactose, and arabinose.

The third stage of the graded hydrolysis of the gum gave a mixture of acidic oligosaccharides. The main component was the aldobiouronic acid, 2-*O*-(β-D-glucopyranosyluronic acid)-D-mannose, whose structure was proved from the following experiments. Hydrolysis of the sugar gave glucuronic acid, glucurone, and mannose. Periodate oxidation gave formaldehyde in low yield (0·3 mol.), presumably owing to incomplete oxidation, but since complete oxidation of the derived glycitol [5] gave only 1 mol. of formaldehyde, the presence of a 2-*O*-substituted mannose residue was suspected. Reduction of the derived methyl ester methyl glycosides with potassium borohydride afforded two neutral components, which were presumably anomeric glycosides since both gave glucose and mannose on hydrolysis and reacted with periodate in a similar manner. The glycoside formed in largest amount was methylated and on subsequent hydrolysis furnished 2,3,4,6-tetra-*O*-methyl-D-glucose and 3,4,6-tri-*O*-methyl-D-mannose. The β-configuration of the glycosidic

[2] Andrews, Hough, and Powell, *Chem. and Ind.*, 1956, 658.
[3] Aspinall, Hirst, and Nicolson, *J.*, 1959, 1697.
[4] Aspinall, Hirst, and Wickstrøm, *J.*, 1955, 1160; Aspinall, Auret, and Hirst, *J.*, 1958, 221, 4408.
[5] Hough, Woods, and Perry, *Chem. and Ind.*, 1957, 1100.

linkage in the aldobiouronic acid may be assigned since the optical rotation ($[\alpha]_D$ −35°) was similar to that ($[\alpha]_D$ −32°) of the aldobiouronic acid from gum ghatti,[4] which has been degraded by Perlin's procedure [6] to 2-*O*-β-D-glucopyranosylglyceritol.[7]

Smaller amounts of other acidic oligosaccharides were partially identified by chromatography of the sugars and their derivatives. One was chromatographically and ionophoretically indistinguishable from 6-*O*-(β-D-glucopyranosyluronic acid)-D-galactose and another was probably a second *O*-(glucosyluronic acid)mannose. Three higher acidic oligosaccharides were composed of glucuronic acid and mannose residues, and may be members of a polymer-homologous series since all gave staining reactions with aniline oxalate similar to that given by 2-*O*-(β-D-glucopyranosyluronic acid)-D-mannose, and the absence of a colour reaction with triphenyltetrazolium hydroxide [8] indicated that in each case the reducing residue was substituted at position 2. One of the oligosaccharides was chromatographically indistinguishable from the aldotriouronic acid, *O*-(D-glucopyranosyluronic acid)-(1 ⟶ 2)-*O*-D-mannopyranosyl-(1 ⟶ 2)-D-mannose, which has been isolated as a partial hydrolysis product from gum ghatti.[7]

The results of this investigation of *Anogeissus schimperi* gum may be compared with those from studies of gum ghatti,[4,7] which is derived from the botanically related species, *Anogeissus latifolia*. The two gums contain L-arabinose, D-galactose, D-mannose, and D-glucuronic acid as the main constituent sugars and, although an exact quantitative comparison of compositions is not possible, it is clear that *A. schimperi* gum contains a substantially higher proportion of D-glucuronic acid and probably also of D-mannose residues. Whereas xylose is only a minor constituent in gum ghatti it is present in substantial proportions in *A. schimperi* gum. In gum ghatti [4] it is probable that this sugar arises from a minor contaminating polysaccharide, and it is possible that in *A. schimperi* gum the xylose is derived from such a second polysaccharide component present in larger amount. Similarly the traces of rhamnose, ribose, and fucose may also be formed from minor contaminants. Even in the absence of proof of homogeneity, it is clear that the two gums contain structural features in common, and the present results may be assessed by considering, in turn, the acid-labile arabinose residues, the framework of D-galactose residues, and the acidic oligosaccharide units.

As in the case of gum ghatti, mild acid hydrolysis of *A. schimperi* gum removes the majority of the L-arabinose residues, and it is probable that these are in the outer parts of the molecular structure and that many are present in the furanose form. The characterisation of 3-*O*-L-arabinofuranosyl-L-arabinose as a partial acid hydrolysis product establishes the presence of adjacent L-arabinose residues in the gum, and chromatographic evidence for the formation of other arabinobioses as partial hydrolysis products indicates that arabinose residues in the gum are mutually linked in a variety of ways. Gum ghatti contains a high proportion of L-arbinose residues as end-groups in the furanose form, but other arbinose residues are present in non-terminal positions linked in a variety of ways.[4] Although no arabinobioses have yet been fully characterised as partial hydrolysis products of gum ghatti, it is probable that the outer chains contain some adjacent arabinose residues since mild acid hydrolysis of the gum removes some of the non-terminal in addition to the terminal L-arabinofuranose units.[4] Furthermore, reduction of the periodate-oxidised gum followed by mild acid hydrolysis affords a degraded gum still containing arabinofuranose end-groups; it is probable that these units have originated from non-terminal arabinose residues in the outer chains, which are also resistant to attack by periodate, since the degradation procedure would remove the outer shell of arabinofuranose end-groups.[7] *A. schimperi* gum, like gum ghatti, contains some arabinose residues in the interior chains

[6] Charlson, Gorin, and Perlin, *Canad. J. Chem.*, 1956, **34**, 1811; Gorin and Perlin, *ibid.*, 1958, **36**, 999.

[7] Christensen, Ph.D. Thesis, Edinburgh, 1960.

[8] Feingold, Avigad, and Hestrin, *Biochem. J.*, 1956, **64**, 351; Bailey, Barker, Bourne, Grant, and Stacey, *J.*, 1958, 1895.

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of the polysaccharide since partial hydrolysis affords the same homologous series of oligosaccharides, *O*-β-D-galactopyranosyl-[(1 → 6)-*O*-β-D-galactopyranosyl]$_n$-(1 → 3)-L-arabinose.

The isolation of the same two series of oligosaccharides containing 1,6-linked β-D-galactopyranose residues from both gums shows that the interior chains are similarly constituted. In contrast, *A. schimperi* gum affords a relatively larger amount of 3-*O*-β-D-galactopyranosyl-D-galactose on partial hydrolysis. There is no evidence yet for the structural environment of these 1,3-linked galactose residues, although it may be noted that no oligosaccharides containing contiguous 1,3-linkages could be detected on partial hydrolysis of the gum.

The two gums furnish different proportions of acidic oligosaccharides, and it is possible that these may reflect not only differences in the proportions of similar structural units, but differences in the types of linkage present. Whereas gum ghatti affords approximately equal proportions of 2-*O*-(β-D-glucopyranosyluronic acid)-D-mannose and 6-*O*-(β-D-glucopyranosyluronic acid)-D-galactose on partial hydrolysis, *A. schimperi* gum affords only the mannose-containing aldobiouronic acid in substantial amount. *A. schimperi* gum also gives rise to 6-*O*-(β-D-glucopyranosyluronic acid)-D-galactose, but this aldobiouronic acid is formed in small amount and hitherto has only been identified by paper chromatography of the sugar and its derivatives. A similar identification of an aldotriouronic acid, *O*-(glucosyluronic acid)-*O*-galactosylarabinose, however, suggests that the galactose glucosiduronic acid units in the gum may be attached to arabinose residues in the outer chains rather than being present as part of the acid-resistant core of the molecular structure. The structural environment of the 2-*O*-(β-D-glucopyranosyluronic acid)-D-mannose units in the gum remains to be fully established, although the isolation of higher acidic oligosaccharides composed of glucuronic acid and mannose residues only indicates that the main aldobiouronic acid are not simply attached to basal chains of galactose residues. The isolation from gum ghatti of similar higher acidic oligosaccharides, including the trisaccharide, *O*-(D-glucopyranosyluronic acid)-(1 → 2)-*O*-D-mannopyranosyl-(1 → 2)-D-mannose,[7] shows that in this respect the two gums have common structural features, and that the molecular structure of gum ghatti is yet more complex than hitherto supposed.[4]

Experimental

Paper chromatography was carried out on Whatman Nos. 1, 3MM, and 31 papers with the following solvent systems (v/v): (A) ethyl acetate–acetic acid–water (3 : 1 : 3, upper layer); (B) ethyl acetate–pyridine–water (10 : 4 : 3); (C) ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4); (D) butan-1-ol–ethanol–water (4 : 1 : 5, upper layer); (E) benzene–ethanol–water (11 : 3 : 1, upper layer); (F) butan-1-ol–ethanol–water (1 : 1 : 1); (G) ethyl acetate–acetic acid–formic acid–water (18 : 8 : 3 : 9); (H) butan-2-one, saturated with water. Paper ionophoresis was in borate buffer at pH 10. Optical rotations were observed for aqueous solutions at 18° ± 2°.

The gum was received from Professor R. J. McIlroy as a light grey powder which had been reprecipitated with ethanol from aqueous solution; it had uronic anhydride (by decarboxylation), *ca.* 22%.

Hydrolysis of the Gum and Identification of Neutral Sugars (with Dr. Barbara J. Auret and Mr. H. Wilkie).—The gum (5 g.) was heated in N-sulphuric acid (300 ml.) on the boiling-water bath for 4 hr. Insoluble material, which separated during the hydrolysis, was filtered off, and the cooled filtrate was neutralised with barium carbonate and filtered. The filtrate was concentrated to a syrup which was poured into methanol (1 l.), precipitated barium salts (1·0 g.) were separated, and the supernatant liquid was concentrated to a syrupy mixture (2·55 g.) of sugars. The sugars were separated on cellulose, with butan-1-ol, half saturated with water, to give six fractions.

Fraction 1 (0·053 g.) contained rhamnose and ribose. Fraction 2 (0·501 g.) had $[\alpha]_D$ +18·7° (equil.), and after recrystallisation from ethanol m. p. and mixed m. p. (with D-xylose) 144°; it was characterised as the di-*O*-benzylidene dimethyl acetal, m. p. and mixed m. p. 210°. Fraction 3 (0·651 g.) had $[\alpha]_D$ +103° (equil.) and, after recrystallisation from methanol, m. p.

159° and mixed m. p. (with L-arabinose) 158°, and was characterised as the benzoylhydrazone, m. p. 187° and mixed m. p. 186°. Fraction 4 (0·681 g.) contained arabinose and traces of mannose. Fraction 5 (0·071 g.) contained D-mannose and L-arabinose in smaller amount; D-mannose was characterised as the phenylhydrazone, m. p. and mixed m. p. 198°. Fraction 6 (0·200 g.) had $[\alpha]_D$ +82° (equil.) and, after recrystallisation from methanol, m. p. and mixed m. p. 168°, and was characterised as the 1-methyl-1-phenylhydrazone, m. p. and mixed m. p. 185°. A sample of the barium salts was dissolved in water, barium ions were removed with Amberlite resin IR-120(H), and chromatographic examination of the resulting solution showed a main component with the mobility of 2-*O*-(β-D-glucopyranosyluronic acid)-D-mannose.

Partial Hydrolysis of the Gum (1).—The gum (23 g.) was heated in 0·01N-sulphuric acid (1600 ml.) on the boiling-water bath for 4 hr., and the cooled solution was neutralised with Amberlite resin IR-4B(OH). The solution was concentrated and poured into ethanol (4 vol.), the precipitated degraded polysaccharide (17 g.) was separated, and the supernatant liquid was concentrated to a syrup (3 g.). The degraded polysaccharide (17 g.) was rehydrolysed under the same conditions and yielded degraded gum A (13 g.) and syrup (2 g.). The combined syrups (5 g.) were separated on cellulose (50 × 3·5 cm.) with butan-1-ol, half saturated with water, as eluant to give four fractions. Fraction 1 (50 mg.) contained rhamnose, ribose, fucose, xylose, and arabinose. Fraction 2 (2·8 g.) contained xylose and arabinose. Fraction 3 (0·41 g.) contained arabinose, oligosaccharides *a* and *b*, and galactose. Fraction 4 (80 mg.) contained oligosaccharides *c*, *d*, *e*, and *f*. Monosaccharides were identified only by paper chromatography; oligosaccharides were further fractionated by chromatography on filter sheets with solvent C.

Oligosaccharide *a* (130 mg.) had $R_{galactose}$ 1·25 in solvent C and $[\alpha]_D$ +107° (*c* 1·0), and gave arabinose only on hydrolysis. Methyl sulphate (1 ml.) and 30% aqueous sodium hydroxide (1 ml.) were added to the sugar (102 mg.) in water (3 ml.) at 0°. Further additions of methyl sulphate (2 × 6 ml.) and 30% sodium hydroxide (2 × 10 ml.) were made at room temperature and the reaction was completed by heating the solution on the boiling-water bath for 1 hr. The methylated oligosaccharide (90 mg.) was isolated by extraction with chloroform. Hydrolysis of a sample (3 mg.) gave tri- and di-*O*-methylarabinoses with only traces of products of incomplete methylation. Hydrolysis of the methylated oligosaccharide (87 mg.) with N-hydrochloric acid at 100° for 5 hr., followed by neutralisation with Amberlite resin IR-45(OH), furnished a syrup (60 mg.) which was separated on cellulose (40 × 1·5 c.) with light petroleum (b. p. 100—120°)–butan-1-ol (7 : 3), saturated with water, as eluant to give five fractions. Fraction (i) (20 mg.), R_G 0·95 in solvent D, was characterised as 2,3,5-tri-*O*-methyl-L-arabinose by conversion into 2,3,5-tri-*O*-methyl-L-arabonamide, identified by m. p. and mixed m. p. 129—131°, and by an *X*-ray powder photograph. Fraction (ii) (5 mg.), R_G 0·83, was chromatographically and ionophoretically indistinguishable from 2,5-di-*O*-methyl-L-arabinose. Fraction (iii) (2 mg.), R_G 0·82 in solvent D, was indistinguishable from 2,3,4-tri-*O*-methyl-L-arabinose in solvent E. Fraction (iv) (14 mg.), R_G 0·60 in solvent D, was chromatographically and ionophoretically indistinguishable from 2,4-di-*O*-methyl-L-arabinose and was characterised by conversion into the aniline derivative, m. p. 148—149° and mixed m. p. (with sample, m. p. 144—146°) 144—145°. Fraction (v) (3 mg.), R_G 0·51 in solvent D, was chromatographically and ionophoretically indistinguishable from 3,4-di-*O*-methyl-L-arabinose. Oligosaccharide *b* (20 mg.), $R_{galactose}$ 1·1 in solvent C, gave arabinose only on hydrolysis. Oligosaccharide *c* (15 mg.), $R_{galactose}$ 0·7 in solvent C, gave arabinose only on hydrolysis and was chromatographically indistinguishable from 3-*O*-β-L-arabinopyranosyl-L-arabinose in solvents, A, B, and C. Oligosaccharide *d* (6 mg.), $R_{galactose}$ 0·55 in solvent C, gave arabinose only on hydrolysis. Oligosaccharide *e* (3 mg.), $R_{galactose}$ 0·5 in solvent C, was stained brown with aniline oxalate (characteristic of substituted hexoses) and yielded mannose and xylose on hydrolysis. Oligosaccharide *f* (10 mg.), $R_{galactose}$ 0·4 in solvent C, was chromatographically indistinguishable from 3-*O*-β-D-galactopyranosyl-L-arabinose.

Partial Hydrolysis of the Gum (2).—The gum (30 g.) was heated in 0·5N-sulphuric acid (1 l.) on the boiling-water bath for 1 hr., and the cooled solution was neutralised to pH 5 with barium hydroxide and subsequently with barium carbonate. Inorganic material was removed at the centrifuge, the solution was concentrated and poured into ethanol (4 vol.), the precipitated degraded polysaccharide was separated, and the supernatant liquid was concentrated to a syrup (10·6 g.). The degraded polysaccharide was rehydrolysed under the same conditions and furnished degraded gum B (8 g.) and syrup (1 g.). The combined syrups (11·6 g.) dissolved in water were adsorbed on charcoal–Celite (1 : 1; 40 × 7 cm.). Elution with water gave

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fraction 1 (9·7 g.) containing xylose, arabinose, galactose, and traces of mannose. Elution with water containing 2·5% of ethanol gave fraction 2 (30 mg.) containing oligosaccharide 1, fraction 3 (30 mg.) containing oligosaccharide 2, and fraction 4 (300 mg.) containing oligosaccharide 3. Elution with water containing 5% of ethanol gave fraction 5 (20 mg.) containing acidic oligosaccharides *a* and *b*, fraction 6 (140 mg.) containing neutral oligosaccharide 4 and acidic oligosaccharides *a* and *b*, and fraction 7 (20 mg.) containing oligosaccharide 5. Elution with water containing 7·5% of ethanol gave fraction 8 (60 mg.) containing oligosaccharide 6, and fraction 9 (50 mg.) containing oligosaccharides 6 and 7, and acidic oligosaccharide *c*. Elution with water containing 10% of ethanol gave fraction 10 (20 mg.) containing oligosaccharide 8, and fraction 11 (10 mg.) containing oligosaccharides 9 and 10. The weights of the fractions are only approximate but give some indication of the relative amounts of pure oligosaccharides, which, in most cases, were isolated after chromatographic separation on filter sheets. Further quantities of several oligosaccharides were isolated in a similar manner after hydrolysis of degraded gum A with 0·5N-sulphuric acid at 100° for four periods of 0·5 hr. (degraded polysaccharide was separated from soluble sugars at the end of each period).

Oligosaccharide 1 had $R_{galactose}$ 0·8 in solvent B and gave arabinose only on hydrolysis. The sugar was indistinguishable from 3-*O*-β-L-arabinopyranosyl-L-arabinose and from oligosaccharide *c* when examined by paper ionophoresis and by paper chromatography in solvents A, B, and C. Hydrolysis of the derived methylated oligosaccharide afforded 2,3,4-tri- and 2,4-di-*O*-methylarabinose.

Oligosaccharide 2, $[\alpha]_D$ +17° (*c* 1·2) and $R_{galactose}$ 0·3 in solvent B, was chromatographically and ionophoretically indistinguishable from 6-*O*-β-D-galactopyranosyl-D-galactose.

Oligosaccharide 3, $R_{galactose}$ 0·6 in solvent B, crystallised and, after recrystallisation from ethanol–water, had $[\alpha]_D$ +97° (2 min.) ⟶ +67° (2 hr., equil.) (*c* 0·45). Hydrolysis of the sugar gave galactose and arabinose, and of the derived glycitol only galactose. The sugar was identified as 3-*O*-β-D-galactopyranosyl-L-arabinose by its m. p. and mixed m. p. 204—205°, and by an *X*-ray powder photograph.

Oligosaccharide 4, $R_{galactose}$ 0·4 in solvent B, crystallised and, after recrystallisation from ethanol–water, had $[\alpha]_D$ +84° (3 min.) ⟶ +61° (3 hr., equil.), m. p. and mixed m. p. 169—170°, and gave an *X*-ray powder photograph identical with that of 3-*O*-β-D-galactopyranosyl-D-galactose.

Oligosaccharide 5, R_F 0·20 in solvent F, was chromatographically indistinguishable from *O*-β-D-galactopyranosyl-(1 ⟶ 6)-*O*-β-D-galactopyranosyl-(1 ⟶ 6)-D-galactose. Partial acid hydrolysis gave galactose and 6-*O*-β-galactopyranosylgalactose.

Oligosaccharide 6, R_F 0·25 in solvent F, gave galactose, arabinose, 3-*O*-β-galactopyranosylarabinose, and 6-*O*-β-galactopyranosylgalactose on partial acid hydrolysis. After recrystallisation from ethanol–water the sugar was identified as *O*-β-D-galactopyranosyl-(1 ⟶ 6)-*O*-β-D-galactopyranosyl-(1 ⟶ 3)-L-arabinose by its m. p. and mixed m. p. 190—191°, and by an *X*-ray powder photograph.

Oligosaccharide 7, R_F 0·12 in solvent F, was chromatographically indistinguishable from the 1,6-linked galactotetraose isolated from gum ghatti.[4] Hydrolysis gave only galactose, and 6-*O*-β-galactopyranosylgalactose was the only disaccharide detected on partial acid hydrolysis.

Oligosaccharide 8, R_F 0·16 in solvent F, gave galactose, arabinose, 3-*O*-β-galactopyranosylarabinose, and 6-*O*-β-galactopyranosylgalactose on partial acid hydrolysis. After recrystallisation from ethanol–water the sugar was identified as *O*-β-D-galactopyranosyl-[(1 ⟶ 6)-*O*-β-D-galactopyranosyl]$_2$-(1 ⟶ 3)-L-arabinose by its m. p. and mixed m. p. 167—172°, and by an *X*-ray powder photograph.

Oligosaccharide 9, R_G 0·075 in solvent F, had an R_M value [9] consistent with that of a 1,6-linked galactopentaose.

Oligosaccharide 10, R_F 0·10 in solvent F, gave galactose, arabinose, 3-*O*-galactopyranosylarabinose, and 6-*O*-galactopyranosylgalactose on partial acid hydrolysis. After recrystallisation from ethanol–water the sugar was identified as *O*-β-D-galactopyranosyl-[(1 ⟶ 6)-*O*-β-D-galactopyranosyl]$_2$-(1⟶ 3)-L-arabinose by its m. p. and mixed m. p. 178—182°, and by an *X*-ray powder photograph.

Acidic oligosaccharides *a* and *b* were chromatographically identified as 2-*O*-(glucosyluronic acid)mannose and 6-*O*-(glucosyluronic acid)galactose.

[9] Bate-Smith and Westhall, *Biochem. Biophys. Acta*, 1950, **4**, 427.

Acidic oligosaccharide c had $[\alpha]_D$ +6° (*c* 0·3) and R_F 0·23 in solvent F and R_F 0·16 in solvent G, and gave a pink stain with aniline oxalate characteristic of reducing pentose derivatives. Hydrolysis gave arabinose, galactose, glucuronic acid, and 6-*O*-(glucosyluronic acid)galactose, and reduction of the derived methyl ester methyl glycosides with potassium borohydride followed by hydrolysis gave arabinose, galactose, and glucose in approximately equal proportions. Hydrolysis of the derived glycitol (borohydride reduction of the acid) gave 6-*O*-(glucosyluronic acid)galactose, galactose (trace), and arabitol.

Partial Hydrolysis of the Gum (3).—Degraded gum B (7·5 g.) was heated in N-sulphuric acid (300 ml.) on the boiling-water bath for 5 hr., the cooled solution was neutralised with barium hydroxide and barium carbonate, and the filtered solution was concentrated to a syrup (5·3 g.). The syrup (5·3 g.) in water was treated with Amberlite resin IR-120(H) to remove barium ions, and the acidic solution was passed through a column of Amberlite resin IR-45(OH) to absorb acids. Elution of the resin with water gave neutral sugars (0·9 g.) and elution with water containing 10% of formic acid afforded a mixture (4·0 g.) of acidic oligosaccharides. Chromatographically pure acidic oligosaccharides I—IV were obtained after separation on filter sheets by using solvent C. Acidic oligosaccharides V and VI, $R_{galactose}$ 0·12 and 0·05 in solvent G, which were not isolated individually, when stained with aniline oxalate showed the same characteristic orange-brown fluorescence in ultraviolet light as acidic oligosaccharides I and IV.

Acidic oligosaccharide I (1·1 g.), $[\alpha]_D$ −35° (*c* 1·85) and $R_{galactose}$ 0·35 and 0·74 in solvents C and G, was chromatographically and ionophoretically indistinguishable from 2-*O*-(glucosyluronic acid)mannose. Hydrolysis gave glucuronic acid, glucurone, and mannose. Oxidation of the sugar with sodium metaperiodate at pH 7·5 gave 0·3 mol. of formaldehyde (estimation by the method of O'Dea and Gibbons [10]). Reduction of the sugar with potassium borohydride, followed by oxidation with periodate, gave 1·0 mol. (constant value) of formaldehyde.

The sugar (0·5 g.) was converted into the methyl ester methyl glycosides by boiling it with methanolic hydrogen chloride for 6 hr. The ester glycosides were treated with potassium borohydride (50 mg.) in methanol (10 ml.) for 24 hr., and two neutral glycoside fractions *a* (150 mg.), $R_{galactose}$ 1·2 in solvent B, and *b* (25 mg.), $R_{galactose}$ 0·8, were isolated after chromatographic separation on filter sheets. Fractions *a* and *b* were probably anomeric disaccharide methyl glycosides since both gave glucose and mannose on hydrolysis and both consumed 2·8 mol. of periodate, and they furnished chromatographically similar products on reduction of the periodate-oxidised glycosides followed by hydrolysis. Fraction *a* (130 mg.) was methylated in the usual way and furnished methylated disaccharide (130 mg.), hydrolysis of which afforded tetra-*O*-methylglucose (R_G 1·0 in solvent D) and tri-*O*-methylmanose (R_G 0·85 in solvent D) with only traces of products of incomplete methylation. The methylated sugars were identified as (i) 2,3,4,6-tetra-*O*-methyl-D-glucose, $[\alpha]_D$ +88·5° (3 min.) ⟶ +77° (3 hr., equil.) (*c* 0·7), by its m. p. and mixed m. p. 81—82°, and by an *X*-ray powder photograph, and (ii) 3,4,6-tri-*O*-methyl-D-mannose, by its m. p. and mixed m. p. 101—103°, and by an *X*-ray powder photograph.

Acidic oligosaccharide II (30 mg.), $R_{galactose}$ 0·25 and 0·67 in solvents C and G, gave glucuronic acid, glucurone, and mannose on hydrolysis. Reduction of the methyl ester methyl glycosides followed by hydrolysis gave glucose and mannose.

Acidic oligosaccharide III (35 mg.), $R_{galactose}$ 0·15 and 0·51 in solvents C and G, was chromatographically and ionophoretically indistinguishable from 6-*O*-(β-D-glucopyranosyluronic acid)-D-galactose. Hydrolysis gave glucuronic acid, glucurone, and galactose, and reduction of the methyl ester methyl glycosides followed by hydrolysis gave glucose and galactose.

Acidic oligosaccharide IV (40 mg.), $R_{galactose}$ 0·07 and 0·32 in solvents C and G, was chromatographically indistinguishable from *O*-(D-glucopyranosyluronic acid)-(1 ⟶ 2)-*O*-D-mannopyranosyl-(1 ⟶ 2)-D-mannose from gum ghatti, and when stained with aniline oxalate gave the same characteristic orange-brown fluorescence in ultraviolet light as acidic oligsaccharide I. Hydrolysis gave glucuronic acid, glucurone, and mannose, and reduction of the methyl ester methyl glycosides followed by hydrolysis gave glucose and mannose.

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[10] O'Dea and Gibbons, *Biochem. J.*, 1953, **55**, 580.

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673. *The Proton Magnetic Resonance Spectra of Porphyrins. Part I. The Effect of β-Substitution* on the Proton Chemical Shifts of Porphyrins.*

By R. J. Abraham, A. H. Jackson, and G. W. Kenner.

Proton magnetic resonance spectra of dications (I) of some porphyrins are summarised in the Table. The chemical shifts are greatly affected by the ring current of the aromatic system, and hence assignments are straightforward. Further, the effect of β-substituents on the chemical shifts of *meso*- and N–H protons can be accounted for by simple addition; in certain cases the arrangement of the β-substituents in isomeric porphyrins ("type isomers") can be assigned from these considerations.

Proton magnetic resonance spectra have been described briefly for solutions of porphyrins in deuterochloroform [1] and trifluoroacetic acid.[2] The present research is an extension of the latter measurements into a systematic survey, including more complex porphyrins derived from natural products.

Porphyrins are very suitable for a detailed proton magnetic resonance study for several reasons. The positions of protons and other substituents around the porphin skeleton are well separated, and therefore, apart from coupling inside a complex substituent, the protons do not interact magnetically. Consequently the spectrum consists merely of single peaks, except for the part due to complex side-chains, and small variations in chemical shifts can be measured directly without any analysis. Also, the large ring current [3] in the porphin nucleus spreads the spectrum out, *e.g.*, the chemical shifts of the *meso*-protons are about 5 p.p.m. to low field of the normal value for olefinic protons and the chemical shifts of the N–H protons are about 12 p.p.m. to high field of the normal value.[1,2] In fact, the spectrum of a porphyrin extends over practically the whole range yet observed in proton magnetic resonance spectroscopy. Assignments of the main groups in the spectrum to varieties of substituent is straightforward.

Elsewhere [4] it will be shown that the chemical shifts observed in porphyrins can be accounted for by a semi-classical calculation of ring currents. In this paper, our theoretical interest is in the connection between small changes in the chemical shifts of *meso*- and N–H protons and alterations of the neighbouring β-substituents; the effects of β-substituents are apparently additive, and, in certain cases, it is possible to predict different spectra for isomers differing only in the "type," [5] *i.e.*, the distribution of the β-substituents. Part III will deal with the effects of substitution in the *meso*-positions.

Experimental

Measurements.—The porphyrins were dissolved (20—70 mg./c.c., 0·03—0·10M, depending on availability) in trifluoroacetic acid (TFA) or deuterotrifluoroacetic acid (DTFA). The spectra were measured at about 25° on a Varian 60 Mc./sec. dual-purpose spectrometer at a usual sweep rate of about 8 c. per sec. per sec. Tetramethylsilane was used as the internal reference, and chemical shifts (see Table) are given on the τ scale. Side-bands were generated from a convenient, large peak, usually that of trifluoroacetic acid or, in the deutero-acid, tetramethylsilane. The position of the trifluoroacetic acid peak (variable from −1·5 to +0·5, cf.

* While the positions occupied in (I) by H_α, H_β, H_γ, and H_δ have been universally described as *meso*, those occupied by R^{1-8} have been described as β and nuclear. We shall use β and also, in conformity with the practice of H. Fischer and others, propionate (Pe) and acetate (A) for the systematically named 2-methoxycarbonylethyl and methoxycarbonylmethyl substituents. Other abbreviations are Pr for n-propyl, Vi for vinyl, TFA for trifluoroacetic acid, and DTFA for deuterotrifluoroacetic acid.

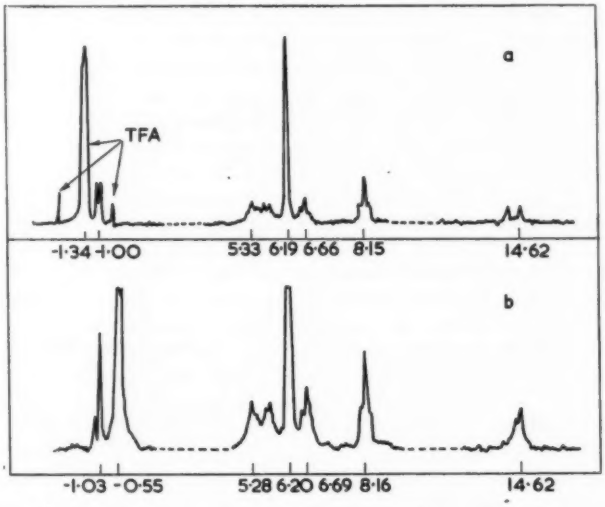
[1] Becker and Bradley, *J. Chem. Phys.*, 1959, **31**, 1413.
[2] Ellis, Jackson, Kenner, and Lee, *Tetrahedron Letters*, 1960, No. 2, 23.
[3] Pople, Schneider, and Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, 1959, p. 180.
[4] Part II, Abraham, *Mol. Phys.*, in the press.
[5] Fischer and Stangler, *Annalen*, 1927, **459**, 62.

Figure) was very sensitive to concentration of the solute, being shifted 0·05 p.p.m. to high field by addition of 1% of tetramethylsilane. Side-bands of trifluoroacetic acid were therefore only used in presence of tetramethylsilane. Each spectrum was measured three times, the mean deviations for the resolved peaks being ±1 c./sec., *i.e.*, ±0·01 p.p.m. The N–H peaks were exceptional in being broader and somewhat dependent on concentration, and the reproducibility of these τ values was about ±0·05 p.p.m. The other values were completely independent of concentration or small changes in the medium.

Materials.—Commercial trifluoroacetic acid was purified by distillation through a short column. Deuterotrifluoroacetic acid was prepared, by vacuum-line techniques, from redistilled trifluoroacetic anhydride and 99·8% deuterium oxide, and the product was purified by fractional distillation under reduced pressure.

The samples of porphin [6] and uroporphyrin II octamethyl ester [7] were kindly supplied by Professor C. Rimington and Dr. S. F. MacDonald, to whom we are grateful. The remaining

Proton magnetic resonance spectra of (a) *mesoporphyrin II dimethyl ester, and* (b) *mesoporphyrin IX dimethyl ester, in trifluoroacetic acid* (TFA) *at* 60 Mc./sec.



compounds were prepared in Liverpool, and we thank P. A. Burbidge, J. Ellis, and P. Johnston, for their assistance with this work, some of which will be included in later publications. The dimethyl esters of mesoporphyrin IX and protoporphyrin IX were prepared from commerical samples of the acids by means of methanolic hydrogen chloride, and they were purified by chromatography in benzene on alumina, followed by crystallisation from chloroform–methanol. Octamethylporphin, ætioporphyrins I and II, and mesoporphyrin II dimethyl ester were prepared from pyrromethenes by essentially classical methods,[8] but the synthesis of coproporphyrin II tetramethyl ester was analogous to that of uroporphyrin II by Arsenault, Bullock, and MacDonald.[7]

Ætioporphyrin III, tetramethyltetrapropylporphyrin III, and coproporphyrin III tetramethyl ester were all prepared by variants [9] of Siedel and Winkler's method.[10] The " type " purity of porphyrins produced by such " non-rational " [11] syntheses from single pyrrole units is still in doubt.[12] However, even the completely random mixture will contain 75% of type

[6] Krol, *J. Org. Chem.*, 1959, **24**, 2065.
[7] Arsenault, Bullock, and MacDonald, *J. Amer. Chem. Soc.*, 1960, **82**, 4384.
[8] Fischer and Orth, " Die Chemie des Pyrrols," Akademische Verlag, Leipzig, 1937, Vol. II, Part I.
[9] Cf. Bullock, Johnson, Markham, and Shaw, *J.*, 1958, 1430.
[10] Siedel and Winkler, *Annalen*, 1943, **554**, 162.
[11] MacDonald and Michl, *Canad. J. Chem.*, 1956, **34**, 1768.
[12] Mauzerall, *J. Amer. Chem. Soc.*, 1960, **82**, 2601, 2605; Morsingh and MacDonald, *ibid.*, p. 4383.

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III and IV isomers,[13] and it should have the same proton magnetic resonance spectrum as either of these isomers according to the theory developed in this paper.

Results and Discussion

Assignments of Spectral Regions.—As porphyrins are diacidic bases,[14] they should exist as dications (I) when dissolved in trifluoroacetic acid. This is confirmed by the area, corresponding to four protons, of the N–H peaks around 14·5. The assignment of these peaks is based on their absence from spectra of solutions in deuterotrifluoroacetic acid. This

Chemical shifts in proton magnetic resonance spectra of porphyrins.

Solutions in trifluoroacetic acid or, where marked *, deuterofluoroacetic acid.

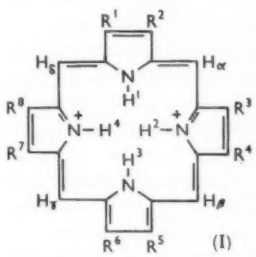
Compound (Substituents of (I))	τ Values of protons								
			β-Substituents						
	N–H	*meso*	CH_3	CH_2–CH_3		CH_2–CH_2–CO_2CH_3			Others
Porphin	14·40								H
R^{1-8} = H	—*	−1·22							0·08
Octamethyl	14·82	−0·98	6·22						
Porphin	—*	−0·98	6·24						
R^{1-8} = Me									
Ætioporphyrin I	14·80	−1·00	6·22	5·70	8·16				
$R^{1, 3, 5, 7}$ = Me	—*	−1·00	6·20	5·70	8·15				
$R^{2, 4, 6, 8}$ = Et									
Ætioporphyrin II	14·81	−1·02	6·19	5·69	8·16				
$R^{1, 4, 5, 8}$ = Me									
$R^{2, 3, 6, 7}$ = Et									
Ætioporphyrin III	14·86	−1·00	6·22	5·71	8·18				
$R^{1, 3, 5, 8}$ = Me									
$R^{2, 4, 6, 7}$ = Et									
Tetramethyltetrapropylporphin III	14·76	−0·98	6·23						CH_2–CH_2–CH_3 5·75 7·73 8·75
$R^{1, 3, 5, 8}$ = Me									
$R^{2, 4, 6, 7}$ = Pr									
Coproporphyrin II tetramethyl ester	14·29	−1·22 (α, γ) −1·06 (β, δ)	6·17			5·27	6·70	6·22	
$R^{1, 4, 5, 8}$ = Me									
$R^{2, 3, 6, 7}$ = Pe									
Coproporphyrin III tetramethyl ester	14·26	−1·12 †	6·17			5·33	6·68	6·22	
$R^{1, 3, 5, 8}$ = Me	—*	−1·21 (γ) −1·11 (α, β) −1·02 (δ)	6·16			5·32	6·65	6·21	
$R^{2, 4, 6, 7}$ = Pe									
Uroporphyrin II octamethyl ester	—*	−1·27 (β, δ) −1·17 (α, γ)				5·29	6·70	6·21	CH_2–CO_2CH_3 4·54 6·12
$R^{1, 4, 5, 8}$ = A									
$R^{2, 3, 6, 7}$ = Pe									
Mesoporphyrin II dimethyl ester	14·36 (1, 3) 14·62 (2, 4)	−1·07 (α, γ) −1·00 (β, δ)	6·19	5·71	8·15	5·33	6·66	6·19	
$R^{1, 3, 5, 7}$ = Me									
$R^{2, 6}$ = Et									
$R^{4, 8}$ = Pe									
Mesoporphyrin IX dimethyl ester	14·48 (3, 4) 14·62 (1, 2)	−1·18 (γ) −1·03 (α, β, δ)	6·19	5·69	8·16	5·28	6·69	6·24	
$R^{1, 3, 5, 8}$ = Me									
$R^{2, 4}$ = Et									
$R^{6, 7}$ = Pe									
Protoporphyrin IX dimethyl ester	14·37	−1·21 (γ) −1·03 (α, β, δ)	6·21			5·32	6·72	6·25	$CH=CH_2$ 1·71 3·43 3·61
$R^{1, 3, 5, 8}$ = Me									
$R^{2, 4}$ = Vi									
$R^{6, 7}$ = Pe									

* In deuterotrifluoroacetic acid. † Partially obscured by solvent.

[13] Cookson and Rimington, *Biochem. J.*, 1954, **57**, 476.
[14] Neuberger and Scott, *Proc. Roy. Soc.*, 1952, *A*, **213**, 307.

exchange between the hydrogen atoms attached to nitrogen and those of the solvent is usually too slow to affect the proton magnetic resonance spectra observed in trifluoroacetic acid. In such cases, the solvent peak is very sharp and the N–H peaks are broad owing to quadrupole relaxation of the nitrogen nuclei.[15] Occasionally, for example, with porphin itself, both the solvent and N–H peaks are very broad, presumably as a result of more rapid exchange, approaching the separation between the peaks[16] (*i.e.*, a proton is attached to a nitrogen atom for about 10^{-4} sec.). This broadening, which became more pronounced in concentrated solutions, made the location of the N–H peak in porphin uncertain to $\pm 0{\cdot}1$ p.p.m. and the N–H peaks of uroporphyrin II octamethyl ester were not detected at all.

The remaining peaks, which are caused by protons attached to carbon atoms, are quite sharp, although still appreciably broader than those from smaller molecules, *e.g.*, impurities,* owing to the relatively slow rotation of the large porphyrin molecules.[17] The Table records spectra of a variety of compounds sufficient to secure the group assignments, and these agree generally with the conclusions of previous workers.[1,2] A new general observation, which we have confirmed with other compounds, is that a proton in a β-position is more shielded than one in a *meso*-position to the extent of 1·3 p.p.m. Calculations[4] of the ring current account for this result and for the displacement of the chemical shifts of all protons on the periphery of the aromatic porphyrin nucleus. As an instance of this displacement, the chemical shift of β-methyl groups is virtually identical with that of the methyl group attached to an oxygen atom in the methyl ester of a carboxylic acid. In compounds containing groups of both kinds, such as the methyl esters of protoporphyrin and mesoporphyrin, the values of the relevant chemical shifts are rendered less certain by this coincidence, but those given are consistent with the other tabulated values. Another complication of the spectra of methyl esters is the gradual appearance at 5·93 of a signal from methyl trifluoroacetate, arising from transesterification of the solvent, but this is only noticeable after the solution has been kept for several weeks at room temperature.



(I)

It is interesting to compare the results from coproporphyrin III tetramethyl ester with those reported by Becker and Bradley[1] for a solution of the same compound in deuterochloroform. The slightly smaller spread in the spectrum of the neutral molecule can be satisfactorily accounted for by the variation in the ring current,[4] in comparison with the more symmetrical dication, but there is a puzzling difference between the peaks corresponding to the *meso*-protons. A singlet is tabulated for the neutral molecule,[1] but a 1 : 2 : 1 triplet is observed in deuterotrifluoroacetic acid solution (only the major peak could be measured in trifluoroacetic acid, as the solvent peak partially obscured the group of *meso*-peaks). Probably the neutral molecules, unlike the dications, are mixtures of tautomers and hence this region of the spectrum may not be so readily resolved. On the other hand, multiplets of unspecified complexity are tabulated for the dimethyl esters of mesoporphyrin IX, protoporphyrin IX, and hæmatoporphyrin IX.

Effects of β-Substituents on the Chemical Shifts of meso-*Protons.*—Spectra of five octaalkylporphyrins are recorded in the Table, and the chemical shifts for all the *meso*-protons are $-1{\cdot}00$ ($\pm 0{\cdot}02$). On the other hand, the value in porphin itself is $-1{\cdot}22$, and hence the effect of alkyl substitution at all the β-positions is to increase the shielding constants for the *meso*-protons by 0·22 p.p.m. Presumably the two β-substituents which are

* The unexplained, sharp peak at 7·7 reported earlier [2] has not been encountered in the present work, and an impurity must have been responsible.

[15] Pople, *Mol. Phys.*, 1958, **1**, 168.
[16] Gutowsky, McCall, and Slichter, *J. Chem. Phys.*, 1953, **21**, 279.
[17] Bloembergen, Purcell, and Pound, *Phys. Rev.*, 1948, **73**, 679; and ref. 3, chapter 9.

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immediate neighbours of a particular *meso*-proton will have the greatest effect on its chemical shift. If this " neighbouring " effect were entirely responsible for the increase in shielding constant noted above, then any *meso*-proton situated between two alkyl groups should have the same chemical shift, irrespective of the rest of the molecule. Although this is unlikely to be true in extreme cases, it is confirmed by the results listed in the Table; in coproporphyrin III tetramethyl ester there is one *meso*-proton (δ) situated between two β-methyl groups and a peak of intensity 1 at −1·02; in both mesoporphyrin II dimethyl ester and coproporphyrin II tetramethyl ester there are two *meso*-protons (β, δ) between β-alkyl substituents and correspondingly peaks of intensity two at −1·02 and −1·06 respectively; and in mesoporphyrin IX dimethyl ester there are three such *meso*-protons (α, β, δ) and a peak of intensity three at −1·03. There is thus good reason to assign these peaks to the corresponding *meso*-protons, and to accept the mean of the ten tabulated values, −1·01 (mean deviation ±0·02), as the expected chemical shift of a *meso*-proton between two β-alkyl substituents. There is some indication that the shielding is reduced by carboxylated side-chains at more remote β-positions, but, if it exists, this effect is apparently of the same order as the experimental error.

In the Table there are five compounds with *meso*-protons situated between two propionate substituents, and in each case there is a peak of the expected intensity in the same region. These peaks are from the γ-protons of coproporphyrin III tetramethyl ester (−1·22), mesoporphyrin IX dimethyl ester (−1·18), and protoporphyrin IX dimethyl ester (−1·21) and the α,γ-protons of coproporphyrin II tetramethyl ester (−1·22) and uroporphyrin II octamethyl ester (−1·17); their mean value is −1·19.

Moreover, there are two examples of *meso*-protons between methyl and propionate substituents, namely the α,β-protons of coproporphyrin III tetramethyl ester and the α,γ-protons of mesoporphyrin II dimethyl ester, and peaks of intensity two are observed at −1·11 and −1·07 respectively. The mean value of −1·09 is consistent with the hypothesis that the effects of the alkyl and propionate substituents are additive. Accepting this hypothesis, we define the contribution of a β-substituent R on the chemical shift of the neighbouring *meso*-proton as R_M and we take porphin itself as the reference compound ($H_M = 0$). Then $Alkyl_M = 0{\cdot}11$ and $Pe_M = 0{\cdot}02$.

Further values can be obtained in the same way. The β,δ-protons of uroporphyrin II octamethyl ester, flanked by acetate groups, are responsible for a peak at −1·27, and hence $A_M = -0{\cdot}03$. The α,β-protons of protoporphyrin IX dimethyl ester lie between methyl and vinyl substituents, and their signal (−1·03) coincides with that of the δ-proton, which is between methyl groups; hence $Vi_M = Me_M = 0{\cdot}11$.

The main importance of these parameters lies in prediction of the relative positions of peaks from *meso*-protons in complex porphyrins. (In so far as β-substitution affects all the *meso*-protons, there may be some discrepancies, but these should concern absolute rather than relative values and the correlation of the tabulated data is very satisfactory.) Some general predictions can be made concerning porphyrins which differ only in the distribution of their β-substituents (" type isomers " [5]). First, in the familiar series where identical pairs of β-substituents, A and B, are distributed on the four pyrrolic rings, the *meso*-protons of type I isomer will give rise to a single peak, those of the type II isomer to two lines of equal intensity, and those of the type III and IV isomers to a triplet of intensity 1 : 2 : 1. The separation of the peaks in the doublet and of the outermost lines in the triplet will be $2(A_M - B_M)$. Provided that A_M and B_M differ sufficiently, proton magnetic resonance provides a simple method of distinguishing isomers, and the spectra of the tetramethyl esters of coproporphyrin II and III illustrate this well.

The analysis can be extended to more complex porphyrins, but a corresponding amount of information cannot always be obtained. For instance, the fifteen mesoporphyrins [5] should give rise to only two patterns; types III, IX, and XIII, which are related to coproporphyrins II, III, and IV, respectively, should have a pair of peaks with intensities three and one in the *meso*-region, while the remaining twelve isomers should have a symmetrical

doublet. The spectra (see Figure) of the dimethyl esters of mesoporphyrin II and IX show this effect. On the other hand, there should be six different patterns from the fifteen isomeric deuteroporphyrins, although it is unlikely that they could all be distinguished experimentally. In combination with the classical methods, proton magnetic resonance spectroscopy should be very useful in distinguishing between particular possibilities.

Effects of β-Substituents on the Chemical Shifts of N–H *Protons.*—The chemical shifts of the N–H protons will be considered in much the same way as the shifts of the *meso*-protons, but the analysis cannot be so definite. On any simple theory, all the octa-alkylporphyrins should show a single N–H peak at the same position. In fact, while single peaks are observed, the five tabulated values spread between **14·76** and **14·86**, but this variation is probably due to experimental uncertainties, *e.g.*, the effect of concentration. If the shift of any given N–H proton is affected only by the two β-substituents attached to the same pyrrole ring, the coproporphyrins should also show a single peak because each ring has a methyl and a propionate substituent; indeed single peaks have been observed at **14·29** and **14·26**. Further, in the mesoporphyrins there should be two equal peaks arising from the rings with methyl-ethyl and methyl-propionate substituents, respectively. Doublets are observed (see Figure) but at approximately **14·6** and **14·4** instead of **14·8** and **14·3**, the positions expected by comparison with the octa-alkylporphins and coproporphyrins. Apparently the assumption of a simple " neighbouring " effect is insufficient, although it does account for the main phenomena. As the basicity of porphyrins, *i.e.*, the acidity of their conjugate acids, is affected considerably by β-substitution [14] and the chemical shift of N–H protons is expected to be connected with their acidity, it is probable that β-substituents have a general effect on the shifts of all four protons in addition to the particular effect in the same pyrrolic ring.

It should also be remarked that protoporphyrin IX, like the mesoporphyrins, should show a doublet, but actually the N–H peak was very broad and fine structure could not be detected.

If fine structure of the N–H peak is observed, the " neighbouring " assumption is likely to be useful despite its limitations, and the following parameters, analogous to those calculated for the *meso*-protons, may serve as an approximate guide to the chemical shifts: $Alkyl_N = 0{\cdot}21$, $Pe_N = 0{\cdot}01$.

Conclusion.—We hope to examine the proton magnetic resonance spectra of a wider variety of porphyrins, including chlorins and degradation products of chlorophyll, and it may be that the correlations deduced from the present data will be modified. Nevertheless, the parameters should serve as a guide to future work, and certain instructive comparisons can be made.

The introduction of a β-methyl substituent increases the chemical shift of the neighbouring *meso*-proton by **0·1** p.p.m. and that of the closest N–H proton by **0·2** p.p.m. In both cases the methyl group is four bonds away from the proton concerned. Figures are not available for the corresponding effect on N–H protons in simple pyrroles, but the introduction of a methyl group at position **2** increases the chemical shift of the **4**-proton, which is again four bonds away, by about **0·2** p.p.m.[18] Thus the mechanism of the shifts may be the same in the pyrrole and the porphyrin series and it could be based on either the inductive effect or the dipole field [19] of the methyl group. The latter mechanism would explain why the effect on a *meso*-proton is smaller. It is in the plane perpendicular to the dipole axis and passing through the dipole, while the N–H proton is close to the dipole axis and therefore experiences a much larger dipole field. It should be noted that substitution of a methyl group at a *meso*-position has a much larger effect, which will be described in Part III, and that there a different mechanism must be involved.

The large decrease in shielding of *meso*- (**0·1** p.p.m.) and N–H (**0·2** p.p.m.) protons, when

[18] Abraham and Bernstein, *Canad. J. Chem.*, 1961, **39**, 905.
[19] Buckingham, *Canad. J. Chem.*, 1960, **38**, 300.

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a β-alkyl substituent is replaced by a propionate group, is at first rather surprising as the carbonyl group is so distant if the side-chain is extended. However, a coiled conformation, in which the side-chain is first bent upwards (the plane of the ring system being taken as horizontal) and then inwards, brings the carbonyl group close to the *meso*-proton and particularly close to the N–H protons. To some extent this conformation can be regarded as the form of lowest energy, because the two polar groups are brought as near to each other as possible. The effect of the carbonyl group may be due to either its dipole field or its magnetic anistropy. Alternatively, the carbonyl group may neutralise the effect of the ethyl substituent, so that it becomes equivalent to a hydrogen atom.

The effect of a β-acetate substituent on the neighbouring *meso*-proton is even larger than that of a propionate substituent, in agreement with the foregoing suggestions. Unfortunately, the value of A_N, which might help to distinguish between them, is not available because the N–H peaks of uroporphyrin II octamethyl ester could not be observed.

It is evident, when the spectra of the dimethyl esters of protoporphyrin IX and mesoporphyrin IX are compared, that the " neighbouring effect " of a vinyl substituent is similar to that of other alkyl groups. Presumably the similarity is due to the non-polar nature of the vinyl group, and it may be that polar conjugative substituents, for instance, aldehyde and ketone groups, will be found to have a more noticeable effect, possibly too great to be accommodated in simple " neighbouring " parameters.

Although the main concern of this paper is with the effects of β-substitution in other parts of the porphyrin molecule, the potential value of proton magnetic resonance in identifying the β-substituents themselves of new porphyrins should not be overlooked. For example, an unsubstituted β-position, like that in cytodeuteroporphyrin,[20] would be apparent from a peak at about 0·1 (τ scale). Again, the signals from a propyl group, a component of chlorobium chlorophyll,[21] are spread out by the ring current so that its detection becomes straightforward. The signals from vinyl groups are very characteristic and displaced from the usual position. A drawback of the proton magnetic resonance method at present is the need for a comparatively large sample (10—30 mg.). The spectra of methyl esters, rather than the corresponding carboxylic acids, are tabulated because the esters were more readily purified, but the acids generally dissolve sufficiently in trifluoroacetic acid and they give similar spectra. In the porphyrin series combustion analysis is frequently not very informative, and we have found our spectra very helpful in counting β-substituents.[22]

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Basic Physics Division, National Physical Laboratory.
Organic Chemistry Department, University of Liverpool. [*Received, February* 14*th*, 1961.]

[20] Marks, Dougall, Bullock, and MacDonald, *J. Amer. Chem. Soc.*, 1960, **82**, 3183.
[21] Holt and Morley, *J. Amer. Chem. Soc.*, 1960, **82**, 500.
[22] Ellis, Jackson, Jain, and Kenner, unpublished work.

674. *Cycloheptatriene– and Tropylium–Metal Complexes. Part I. The "Normal" Reaction of Tricarbonyltropyliumchromium Salts with Anions.*

By J. D. Munro and P. L. Pauson.

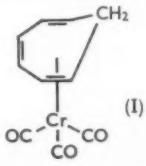
Conversion of tricarbonylcycloheptatrienechromium into tricarbonyltropyliumchromium perchlorate is described. The latter reacts with most anions to give 7-substituted tricarbonylcycloheptatrienechromiums. Numerous examples of this, the "normal" mode of reaction, are given and the analogous behaviour of the corresponding molybdenum compounds is demonstrated.

At the outset of the present work the reaction of cycloheptatriene with chromium and molybdenum hexacarbonyls had been shown to give tricarbonylcycloheptatriene-chromium (I) and -molybdenum, respectively,[1] and the latter had been converted into the tricarbonyltropylium-molybdenum cation.[2] We now report on the reactions of the latter and more particularly of the analogous tricarbonyltropyliumchromium cation (II) with various anions. *A priori*, this cation may be expected to react with anions in one of two ways.

Mode 1: $[C_7H_7Cr(CO)_3]^+ + X^- \longrightarrow XC_7H_7Cr(CO)_3$

Mode 2: $[C_7H_7Cr(CO)_3]^+ + X^- \longrightarrow C_7H_7Cr(CO)_2X + CO$

Mode 1 assumes that the positive charge resides largely on the seven-membered ring and that anions can add to this ring as they do to free tropylium ions. It is in fact the mode of reaction most frequently observed by us and is therefore referred to in the present paper as the "normal" reaction.



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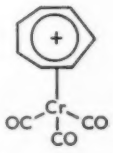
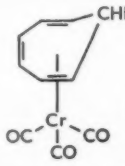


(II)



(III)

Mode 2 assumes that sufficient of the charge is located on the metal atom for anionic attack at this point and is based on the analogy with the behaviour [3] of the tricarbonylbenzenemanganese cation with cyanide:

$$[C_6H_6Mn(CO)_3]^+ + CN^- \longrightarrow C_6H_6Mn(CO)_2{\cdot}CN + CO$$

Our investigation was prompted by the hope that reaction of cyclopentadienide ion by essentially this mode might lead to cycloheptatrienylcyclopentadienylchromium, isomeric with dibenzenechromium. This expectation was not realised, but the interesting rearrangement observed with cyclopentadienide ions is reported in detail in the following paper. It is possible, however, that the "abnormal" base reaction described in Part III is initiated by a step, essentially following mode 2.

The starting material (II) may be obtained as the fluoroborate from the cycloheptatriene complex (I) in the same manner as its molybdenum analogue, but is more conveniently prepared as the perchlorate by using triphenylmethyl perchlorate. Owing to the difficulties in analysing either of these salts, the reineckate and tri-iodide were employed for more complete characterisation. Tricarbonylmethyltropyliumchromium perchlorate and the corresponding tri-iodide were prepared similarly. Although tricarbonyltropyliummolybdenum perchlorate may be prepared by the same method, it, unlike the chromium analogue, is rather explosive.

[1] Abel, Bennett, Burton, and Wilkinson, *J.*, 1958, 4559.
[2] Dauben and Honnen, *J. Amer. Chem. Soc.*, 1958, **80**, 5570.
[3] Coffield and Closson, Abs. 134th Amer. Chem. Soc. Meeting, 1958, 58P.

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In the present paper we describe the " normal " reaction of the tricarbonyltropyliumchromium perchlorate with the hydride, methoxide, hydrogen sulphide, t-butylcyclopentadienide and diethyl methylmalonate ions. These lead to the products [III; R = H, OMe, SH, $C_5H_4{\cdot}CMe_3$, $CMe(CO_2Et)_2$] in which the substituent R can be on the same (*cis*) or the opposite side (*trans*) of the ring from the chromium atom. Attempts to decide between these alternative stereochemical formulations are in progress. All the products obtained were crystalline and possessed sharp melting points and are therefore undoubtedly pure and probably all of the same configuration.

The tricarbonyltropylium-molybdenum ion is much less stable under the reaction conditions employed in the chromium series, but at least the reactions with borohydride and diethyl sodiomalonate have been shown to proceed in the same manner.

Since phenyl-lithium did not react with the tropyliumchromium ion (cf. Part III, below) according to the " normal " mode of reaction, we attempted to obtain tricarbonylphenylcycloheptatrienechromium by the method of Abel *et al.*[1] from phenylcycloheptatriene. These authors give no physical properties or analyses for their product. Even after careful chromatography we failed to obtain a pure compound. The main fraction gave correct analyses but melted over a wide temperature range and was presumably a mixture of stereo- and/or position isomers. Contrary to the impression given by the earlier workers, it was accompanied by material, which from its infrared spectrum was clearly tricarbonylcycloheptatrienylbenzenechromium; this likewise was only obtained as a gummy mixture of isomers. The proportions of these two types of product may well depend on the reaction time, since we were readily able to displace cycloheptatriene from its tricarbonylchromium complex with, for example, mesitylene. This is in harmony with the ready displacement of cycloheptatriene from this complex by phosphines,[1,4] amines,[4] sulphides,[5] etc., and of one arene by another in tricarbonylbenzenechromium derivatives.[6]

Experimental

M. p.s were determined in sealed, evacuated capillaries. Ligroin refers to the solvent of b. p. 60—80°. Alumina employed for chromatography was Spence's " grade H " which had been partially deactivated by exposure to air for 6 hr. All reactions were carried out under nitrogen.

Tricarbonylcycloheptatrienechromium (I).—Cycloheptatriene (6 g., 0·065 mole) and chromium hexacarbonyl (5 g., 0·023 mole) were refluxed in diethylene glycol dimethyl ether (25 ml.) for 14 hr. After the removal of solvent under reduced pressure, the product (3·16 g., 64%) was crystallised from ligroin. Tricarbonylcycloheptatrienechromium formed deep red needles, m. p. 129—130° (lit.,[1] m. p. 128—130°), soluble in all common organic solvents (Found: C, 52·6; H, 3·6; O, 20·7. Calc. for $C_{10}H_8CrO_3$: C, 52·6; H, 3·5; O, 21·0%).

Conversion into Tricarbonylmesitylenechromium.—Tricarbonylcycloheptatrienechromium (1 g., 0·0044 mole) and mesitylene (10 ml.) were refluxed for 24 hr. The excess of mesitylene was removed *in vacuo* and the yellow residue (0·93 g.) dissolved in ligroin and chromatographed on alumina (40 g.). Elution with ligroin gave unchanged tricarbonylcycloheptatrienechromium (14·1 mg.). This was closely followed by a second band, which yielded tricarbonylmesitylenechromium (0·74 g., 66%) as yellow needles, m. p 168—169° (lit.,[7] m. p. 172—174°), soluble in all common organic solvents (Found: C, 56·2; H, 4·9. Calc. for $C_{12}H_{12}CrO_3$: C, 56·2; H, 4·7%).

Tricarbonyltropyliumchromium Salts (II).—Tricarbonylcycloheptatrienechromium (0·4 g., 0·00175 mole) was dissolved in methylene chloride (10 ml.) and triphenylmethyl fluroroborate [8] (0·67 g., 0·002 mole) in the same solvent (15 ml.) was added. The product was precipitated (0·53 g., 99%) and recrystallised from acetone as orange needles, which darken above 230° but do not melt below 300° (Found: C, 39·3; H, 2·5. $C_{10}H_7BCrF_4O_3$ requires C, 38·3; H, 2·3%).

[4] Abel, Bennett, and Wilkinson, *J.*, 1959, 2323.
[5] Cotton and Zingales, *Chem. and Ind.*, 1960, 1219.
[6] Natta, Ercoli, Calderazzo, and Santambrogio, *Chimica e Industria*, 1958, **40**, 1003.
[7] Jackson, Nicholls, and Whiting, *J.*, 1960, 469.
[8] Dauben, Honnen, and Harmon, *J. Org. Chem.*, 1960, **25**, 1442.

Tricarbonyltropyliumchromium tetrafluoroborate is soluble in water, very slightly soluble in methylene chloride, and insoluble in ligroin, benzene, or ether.

Tricarbonyltropyliumchromium perchlorate (1·25 g., 97%) was prepared similarly by using triphenylmethyl perchlorate in place of the fluoroborate. It crystallised from acetone, forming red needles which darken above 270° but do not melt below 300°. It exploded violently during attempted carbon–hydrogen analysis and is readily detonated by friction. The compound is soluble in water, very sparingly soluble in methylene chloride, ether, and tetrahydrofuran, and insoluble in ligroin or benzene.

An aqueous solution of the perchlorate on treatment with a saturated solution of Reinecke's salt quantitatively precipitated the *reineckate*, which formed orange needles from acetone (Found: C, 29·7; H, 2·7; O, 9·3; N, 15·6. $C_{14}H_{13}Cr_2N_6O_3S_4$ requires C, 30·8; H, 2·4; O, 8·8; N, 15·4%). Tricarbonyltropyliumchromium reineckate decomposes above 280°, but does not melt below 320°; it is slightly soluble in alcohol and insoluble in non-polar solvents.

The *tri-iodide* was quantitatively precipitated when an aqueous solution of the perchlorate was treated with an excess of a solution of potassium tri-iodide. Tricarbonyltropyliumchromium tri-iodide forms brown needles (from acetone) which decompose above 150° (Found: C, 19·7; H, 1·2; O, 7·8; I, 62·9. $C_{10}H_7CrI_3O_3$ requires C, 19·7; H, 1·2; O, 7·9; I, 62·4%). It is insoluble in non-polar solvents and slightly soluble in alcohol.

Tricarbonylmethyltropyliumchromium Perchlorate.—Tricarbonylmethylcycloheptatrienechromium [1] (1 g., 0·0041 mole) in methylene chloride (8 ml.) was treated with triphenylmethyl perchlorate (2 g., 0·0058 mole) in the same solvent (25 ml.). Tricarbonylmethyltropyliumchromium perchlorate was quantitatively precipitated and formed red needles (from acetone) which darken above 270° but do not melt below 300°. It is soluble in water, very sparingly soluble in methylene chloride, ether, and tetrahydrofuran and insoluble in ligroin or benzene. For characterisation, an aqueous solution of the perchlorate was treated with aqueous potassium tri-iodide in excess. The precipitated *tricarbonylmethyltropyliumchromium tri-iodide* crystallised from acetone as brown needles, which decomposed from 150° but did not melt below 320° (Found: C, 21·5; H, 1·6. $C_{11}H_9CrI_3O_3$ requires C, 21·2; H, 1·5%).

Tricarbonyltropylium-molybdenum Salts.—Tricarbonylcycloheptatrienemolybdenum [1] (1 g., 0·0037 mole) was treated with triphenylmethyl perchlorate (1·5 g., 0·0044 mole) in methylene chloride (50 ml.). A precipitate of *tricarbonyltropylium-molybdenum perchlorate* (1·29 g., 95%) was obtained immediately. Recrystallisation from acetone gave orange needles, which decompose explosively at ~80°, are soluble in water, sparingly so in methylene chloride, ether, and tetrahydrofuran, and insoluble in ligroin or benzene. The compound is readily detonated by heat and friction.

An aqueous solution of the perchlorate was treated with an excess of a solution of Reinecke's salt and a quantitative yield of the *reineckate* was obtained. Recrystallisation from acetone gave orange plates, which decompose above 170° but do not melt below 300° (Found: C, 28·7; H, 2·2; N, 14·1. $C_{14}H_{13}CrMoN_6O_3S_4$ requires C, 28·5; H, 2·2; N, 14·3%). The compound is insoluble in water and only slightly soluble in alcohol or methylene chloride.

The *tri-iodide* was quantitatively precipitated when an aqueous solution of the perchlorate was treated with an excess of potassium tri-iodide. The crystals were washed with carbon tetrachloride to remove free iodine and recrystallised from acetone as brown plates, which decompose from 100° but do not melt below 320° (Found: C, 18·5; H, 1·2. $C_{10}H_7I_3MoO_3$ requires C, 18·8; H, 1·1%). It is insoluble in water, but slightly soluble in alcohol or methylene chloride.

Reduction of Tricarbonyltropyliumchromium Perchlorate by Sodium Borohydride.—Sodium borohydride (0·38 g., 0·01 mole) was added, with stirring, to a solution of tricarbonyltropyliumchromium perchlorate (1 g., 0·0031 mole) in water (250 ml.) at room temperature. The resulting mixture was set aside for 10 min. and then extracted with ether. The ether extract was dried (Na_2SO_4) and evaporated to dryness, leaving a red solid (0·41 g.), which was dissolved in ligroin and chromatographed on alumina (20 g.). Elution with ligroin gave tricarbonylcycloheptatrienechromium (0·39 g., 56%) as deep red needles, m. p. 129—130°, identified by mixed m. p. and infrared comparison with an authentic sample.

Reduction of Tricarbonyltropylium-molybdenum Perchlorate by Sodium Borohydride.—Tricarbonyltropylium-molybdenum perchlorate (0·74 g., 0·002 mole) in water (250 ml.) was stirred with sodium borohydride (0·19 g., 0·005 mole) at room temperature for 10 min. The resulting mixture was extracted with ether, and the dried (Na_2SO_4) extract evaporated to dryness leaving

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a red solid (0·168 g., 31%). Recrystallisation from ligroin yielded red plates of tricarbonylcycloheptatrienemolybdenum, m. p. and mixed m. p. 100—101°.

Tricarbonyl-7-methoxycyclohepta-1,3,5-trienechromium (III; R = OMe).—Tricarbonyltropyliumchromium perchlorate (1 g., 0·0031 mole), suspended in methanol (20 ml.), was added to a solution from sodium (0·2 g., 0·0087 g.-atom) in methanol (10 ml.). The mixture was stirred for 2 hr., the solvent was removed under reduced pressure, and the residue extracted with ligroin. Evaporation of the ligroin extract yielded *tricarbonyl-7-methoxycyclohepta-1,3,5-trienechromium* (0·695 g., 88%), crystallising from the same solvent as orange needles, m. p. 107—109° (Found: C, 51·3; H, 4·0; OMe, 11·9. $C_{11}H_{10}CrO_4$ requires C, 51·2; H, 3·9; OMe, 12·0%).

When this compound was treated with triphenylmethyl perchlorate, tricarbonyltropyliumchromium perchlorate was obtained in quantitative yield and was identified by infrared comparison with an authentic specimen and by reduction with sodium borohydride to tricarbonylcycloheptatrienechromium, m. p. and mixed m. p. 129—130°.

Tricarbonyl-7-mercaptocyclohepta-1,3,5-trienechromium (III; R = SH) *and Hexacarbonyl(ditropyl Disulphide)bischromium.*—Hydrogen sulphide was bubbled through a mixture of tricarbonyltropyliumchromium perchlorate (1 g., 0·0031 mole) in water (200 ml.) and sodium hydrogen sulphide (0·34 g., 0·006 mole) in water (5 ml.) for 8 hr. The precipitated solid (0·52 g.) was then filtered off and dissolved in ether, the solution dried (Na_2SO_4), and the ether evaporated. The red residue (0·395 g.) was dissolved in ligroin–benzene (1 : 1) and chromatographed on alumina (170 g.), giving two bands. Elution with the same solvent gave *hexacarbonyl(ditropyl disulphide)bischromium* (0·27 g., 35%) as orange-red crystals (from ligroin–ether) (Found: C, 46·3; H, 2·9. $C_{20}H_{14}Cr_2O_6S_2$ requires C, 46·3; H, 2·7%). The compound decomposes from about 78° without melting and is soluble in ether, benzene, and acetone and only very slightly soluble in ligroin. The second band decomposed on the column before it could be eluted.

In a second experiment, the red ether extract was concentrated and an orange solid, which decomposed from 60° and melted to a red liquid at 70—71°, was obtained. The existence of a thiol group in this product was shown by the strong infrared absorption at 2658 cm.$^{-1}$. Recrystallisation of tricarbonyl-7-mercaptocyclohepta-1,3,5-trienechromium from ligroin–ether was accompanied by oxidation to the above disulphide.

Extraction of the red reaction mixture with dilute aqueous sodium hydroxide gave an orange extract, but attempts to isolate the thiol from this alkaline solution were unsuccessful.

Tricarbonyl-7-[1,1-di(ethoxycarbonyl)ethyl]cyclohepta-1,3,5-trienechromium (III; R = $CMe(CO_2Et)_2$].—Tricarbonyltropyliumchromium perchlorate (2 g., 0·0062 mole) and diethyl sodiomethylmalonate (2·36 g., 0·012 mole) [prepared from sodium (0·276 g., 0·012 g.-atom), ethyl alcohol (10 ml.), and diethyl methylmalonate (2·8 g., 0·016 mole)] in tetrahydrofuran (50 ml.) were allowed to react at room temperature overnight. The solvent was distilled off *in vacuo* and the red residue extracted with ligroin. Chromatography on neutralised alumina gave a single red band of *tricarbonyl-7-[1,1-di(ethoxycarbonyl)ethyl]cyclohepta-1,3,5-trienechromium* (1·94 g., 79%), eluted with ligroin–benzene (1 : 1). Recrystallisation from ligroin gave red plates, m. p. 91—92° (Found: C, 54·1; H, 5·0. $C_{18}H_{20}CrO_7$ requires C, 54·0; H, 5·0%). No tricarbonylbenzenechromium could be detected.

When this ester (1·2 g., 0·003 mole) had been refluxed in methanolic 10% potassium hydroxide (30 ml.) for 3 hr., filtration of the mixture gave a yellow potassium salt (0·5 g.), which showed strong absorption at 1996, 1876, and 1653 cm.$^{-1}$ in the carbonyl stretching frequency region and became brown in air. Acidification with 2N-hydrochloric acid (5 ml.) of its aqueous solution (30 ml.), extraction with ether (250 ml.), and evaporation of the dried ($MgSO_4$) ether extract yielded only a yellow liquid (164 mg.), which decomposed in air.

Tricarbonyl-7-[di(ethoxycarbonyl)methyl]cycloheptatrienemolybdenum (with G. H. Smith).—Sodium (0·12 g., 0·0052 g.-atom) in ethanol (5 ml.) was added to an excess of diethyl malonate (5 ml.) in tetrahydrofuran. Tricarbonyltropylium-molybdenum fluoroborate (1·83 g. 0·0051 mole) was then added and the mixture shaken for 30 min. After removal of solvents and unchanged diethyl malonate under reduced pressure, the solid residue was extracted with n-pentane (25 ml.). On concentration of the extract, *tricarbonyl-7-[di(ethoxycarbonyl)methyl]-cycloheptatrienemolybdenum* (0·725 g., 33%) separated as red needles, m. p. 92—93° (Found: C, 47·6; H, 4·4. $C_{17}H_{18}MoO_7$ requires C, 47·45; H, 4·2%).

Tricarbonyl-7-[5(?)-t-butyl-5-cyclopentadienyl]cycloheptatrienechromium (III; R = Bu^t).—Dimethylfulvene (0·7 g., 0·0066 mole) in ether (10 ml.) was added dropwise to methyl-lithium

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[prepared from methyl iodide (1 g., 0·007 mole) and lithium metal (0·11 g., 0·016 g.-atom) in ether (7 ml.)] with cooling. Tricarbonyltropyliumchromium perchlorate (0·43 g., 0·0013 mole) was then added, resulting in the immediate formation of a deep red colour and the liberation of heat. The mixture was left overnight, the solvent removed under reduced pressure, and the red residue extracted with ligroin. Chromatography of this extract on alumina (40 g.) and elution with the same solvent afforded three bands. One yielded only a trace of a yellow oil and the second a trace of a red gum. From the third band, *tricarbonyl-t-butylcyclopentadienylcycloheptatrienechromium* (63 mg., 14·4%) was obtained, crystallising from ligroin as red needles, m. p. 129—130° (Found: C, 65·4; H, 6·1. $C_{19}H_{20}CrO_3$ requires C, 65·5; H, 5·9%). It is soluble in all common organic solvents.

Reaction of Phenylcycloheptatriene with Chromium Hexacarbonyl.—Phenylcycloheptatriene [9] (4 g., 0·02 mole) was heated with chromium hexacarbonyl (5 g., 0·023 mole) in diethylene glycol dimethyl ether (15 ml.) at 120° for 6 hr. The solvent was then removed *in vacuo* and the residue chromatographed on alumina with ligroin as solvent. This eluted a first orange band from which a red uncrystallisable gum (24 mg.) was obtained. The second scarlet band afforded a deep red gum (0·51 g.). This solidified partly to a red solid, m. p. 60—72°, on trituration with a mixture of ligroin and ether. Recrystallisation from the same solvent mixture raised the melting range to 71—77° (0·42 g., 6·05%), but a product possessing a sharp m. p. could not be obtained in this way. The product is probably a mixture of several isomers of *tricarbonylphenylcycloheptatrienechromium* (Found: C, 63·5; H, 4·3. $C_{16}H_{12}CrO_3$ requires C, 63·2; H, 4·0%). The third yellow band afforded a yellow gum (0·12 g.) which failed to crystallise from a number of solvents and did not sublime. The presence of tricarbonylcycloheptatrienylbenzenechromium in this fraction is indicated by the strong absorption at 1962 and 1889 cm.$^{-1}$ (CCl_4 solution) in the metal–carbonyl stretching frequency region.

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[9] Doering and Knox, *J. Amer. Chem. Soc.*, 1954, **76**, 3203.

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675. *Cycloheptatriene- and Tropylium-Metal Complexes. Part II.*[1] *The Rearrangement to Benzene Complexes.*

By J. D. MUNRO and P. L. PAUSON.

Sodio-cyclopentadiene or -diethyl malonate causes ring contraction of tricarbonyltropyliumchromium (and molybdenum) salts, giving tricarbonylbenzenechromium. By substitution with tritium and methyl it is shown that the benzene ring is derived entirely from the cycloheptatrienyl ring by extrusion of a carbon atom. The formation of intermediate addition products is demonstrated and a tentative mechanism for the ring contraction is proposed.

As we have reported briefly elsewhere,[2] reaction of tricarbonyltropyliumchromium perchlorate (I) with an excess of cyclopentadienide ion does not follow the " normal " mode established for a variety of other anions in the preceding paper,[1] but affords tricarbonylbenzenechromium (II). The molybdenum analogue behaves similarly. The reaction may be represented formally as:

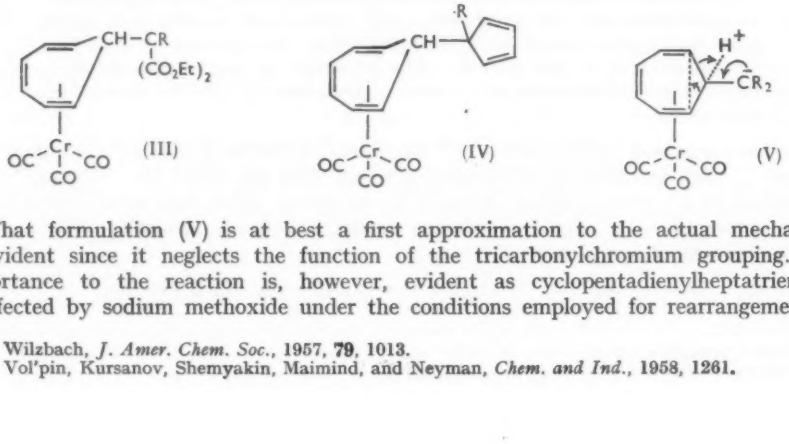
$$\underset{\text{(I)}}{[C_7H_7Cr(CO)_3]^+ClO_4^-} + C_5H_5^-Na^+ \longrightarrow \underset{\text{(II)}}{C_6H_6Cr(CO)_3} + C_6H_6 + NaClO_4 \quad \ldots \quad (1)$$

[1] Part I, preceding paper.
[2] Munro and Pauson, *Proc. Chem. Soc.*, 1959, 267.

This equation shows that two C_6 fragments may be generated. It was therefore considered necessary to establish whether the benzene ring attached to chromium in the product was derived entirely from the seven-membered ring or in part from the cyclopentadiene ring. A decision in favour of the former view was reached qualitatively by repeating the reaction first with methylcyclopentadienylsodium, whereupon the benzene derivative (II) was again the only chromium complex isolated; then, with tricarbonylmethyltropylium chromium,[1] tricarbonyltoluenechromium was obtained. The conclusion was corroborated more quantitatively by labelling the tropylium complex (I) with tritium and showing that the derived product (II) contained the expected proportion of tritium. Tritium-labelled tricarbonylcycloheptatrienechromium required for this purpose was readily prepared by the Wilzbach technique.[3] As in other examples of this method and notwithstanding the fact that the unsaturated system in our compound is a complex with a metal atom, we observed that the replacement by tritium of the olefinic protons far exceeded replacement of the methylene hydrogen atoms.

The same ring-contraction was again observed when the tropylium complex (I) was treated with an excess of diethyl sodiomalonate. The simultaneous isolation of tricarbonyl-7-di(ethoxycarbonyl)methylcycloheptatrienechromium (III; R = H) suggested that the "normal" anion addition[1] is an intermediate step in these rearrangements. This was confirmed by showing that the ester (III; R = H) is transformed into the benzene complex (II) by the further action of sodiomalonate or other bases such as sodium methoxide. The corresponding intermediate (IV) in the cyclopentadienide reaction was readily isolated when an excess of the tropylium complex (I) was used and was similarly transformed into tricarbonylbenzenechromium (II) by methoxide ion. This complex (IV) had a wide melting range and must be assumed to be a mixture of stereo- (and/or position) isomers. A non-crystalline but otherwise closely similar product (IV) was prepared from cyclopentadienylcycloheptatriene[4] and chromium hexacarbonyl. That the methylmalonate complex (III; R = Me) fails to rearrange indicates that ionisation of the acidic hydrogen (R in III and IV) induced by the basic catalyst is an essential step in the ring contraction. It is for this reason that the t-butylcyclopentadienyl derivative obtained previously[1,2] without ring-contraction is now tentatively formulated as (IV; R = Bu^t).

The above observations lead us to propose that the electronic shifts indicated in (V) represent a possible mechanistic picture for this ring-contraction. On this basis the "C_6H_6" fragment in reaction (1) would be fulvene, and diethyl methylenemalonate would result similarly from (III; R = H). Neither of these products has been isolated, nor indeed would they be expected to survive the reaction conditions, but attempts are in progress to find a case where the corresponding product may be isolated.



That formulation (V) is at best a first approximation to the actual mechanism is evident since it neglects the function of the tricarbonylchromium grouping. Its importance to the reaction is, however, evident as cyclopentadienylheptatriene is unaffected by sodium methoxide under the conditions employed for rearrangement of

[3] Wilzbach, *J. Amer. Chem. Soc.*, 1957, **79**, 1013.
[4] Vol'pin, Kursanov, Shemyakin, Maimind, and Neyman, *Chem. and Ind.*, 1958, 1261.

its complex (IV). In this connection we also treated tricarbonyltropyliumchromium perchlorate (I) with silver oxide and with aqueous hydrogen peroxide under the conditions under which these reagents convert the free tropylium ion into benzaldehyde [5] and benzene [6,7] respectively. However, only the same metal-free products were isolated and it is not known whether ring-contraction preceded or followed cleavage of the hydrocarbon fragment from the metal.

Experimental

For general remarks see Part I (preceding paper).

Reaction of Tricarbonyltropyliumchromium Perchlorate (I) *with an Excess of Cyclopentadienide.*—(*a*) Tricarbonyltropyliumchromium perchlorate (2·80 g., 0·0086 mole), suspended in tetrahydrofuran (50 ml.), was added to sodium cyclopentadienide prepared in the same solvent [from sodium wire (0·5 g., 0·022 mole) and cyclopentadiene (7 ml.)]. The mixture was stirred at room temperature overnight. Removal of solvent *in vacuo*, extraction with ether, evaporation, and sublimation at 50°/0·01 mm. of the residue afforded yellow needles of tricarbonylbenzenechromium (0·86 g., 46%), m. p. 162—163° (lit.,[8] m. p. 161·5—163°) [Found: C, 50·4; H, 2·6; O, 21·8%; *M* (cryoscopic in benzene), 215. Calc. for $C_9H_6CrO_3$: C, 50·5; H, 2·8; O, 22·4%; *M*, 214]. Identity was established by mixed m. p. determination and infrared comparison with an authentic sample.

(*b*) Butyl-lithium (0·006 mole) was prepared from butyl bromide (0·82 g., 0·006 mole) and lithium (0·07 g., 0·01 g.-atom) in light petroleum (10 ml.) at room temperature. Cyclopentadiene (3 ml.) was added dropwise and the mixture stirred at room temperature for 2 hr. Tricarbonyltropyliumchromium perchlorate (1 g., 0·0031 mole) in tetrahydrofuran (30 ml.) was then added and the mixture stirred overnight at room temperature. The solvent was removed *in vacuo* and the residue extracted with ligroin. Evaporation of the ligroin extract gave yellow needles of tricarbonylbenzenechromium (0·204 g., 31%), m. p. 162—163°, identified by mixed m. p. and infrared comparison with an authentic specimen.

Reaction of Tricarbonyltropyliummolybdenum Perchlorate with an Excess of Sodium Cyclopentadienide.—Tricarbonyltropyliummolybdenum perchlorate (2·2 g., 0·006 mole) was treated with sodium cyclopentadienide as described under (*a*) above. The solvent was removed under reduced pressure and the residue extracted with ligroin (2 × 100 ml.). Evaporation of the extract *in vacuo* and rapid recrystallisation of the residue from ligroin gave yellow crystals (0·21 g., 14%), m. p. 118—124° (decomp.) (lit.,[9] m. p. 120—125°), identified as tricarbonylbenzenemolybdenum by mixed m. p. and infrared comparison.

Reaction of Tricarbonyltropyliumchromium Perchlorate with an Excess of Sodium Methylcyclopentadienide.—Sodium methylcyclopentadienide (0·006 mole) was prepared by stirring sodium wire (0·14 g., 0·006 g.-atom) and methylcyclopentadiene (0·5 g., 0·006 mole) in tetrahydrofuran (30 ml.) for 3 hr. at room temperature. Tricarbonyltropyliumchromium perchlorate (1 g., 0·0031 mole) was added and the mixture stirred overnight. The solvent was then distilled *in vacuo* and the brown residue extracted with ligroin. Evaporation of the extract to dryness gave yellow crystals of tricarbonylbenzenechromium (0·286 g., 44%), m. p. and mixed m. p. 162—163°.

Reaction of Tricarbonylmethyltropyliumchromium Perchlorate with an Excess of Sodium Cyclopentadienide.—An excess of sodium cyclopentadienide [from cyclopentadiene (2 ml.) and sodium wire (0·2 g., 0·0087 g.-atom)] in tetrahydrofuran (40 ml.) was added at room temperature to a suspension of tricarbonylmethyltropyliumchromium perchlorate [1] (0·8 g., 0·00236 mole) in tetrahydrofuran (30 ml.), and the mixture stirred overnight. After removal of solvent under reduced pressure, the residue was extracted with ligroin. Evaporation of the extract and recrystallisation from the same solvent yielded tricarbonyltoluenechromium (0·28 g., 52%) as bright yellow needles, m. p. and mixed m. p. 81—82° (lit.,[8] m. p. 80—81°) (Found: C, 52·7; H, 3·7. Calc. for $C_{10}H_8CrO_3$: C, 52·7; H, 3·5%).

[5] Doering and Knox, *J. Amer. Chem. Soc.*, 1957, **79**, 354.
[6] Vol'pin and Kursanov, *Doklady Akad. Nauk S.S.S.R.*, 1959, **126**, 780.
[7] Vol'pin, Kursanov, and Dulova, *Tetrahedron*, 1960, **8**, 33.
[8] Jackson, Nicholls, and Whiting, *J.*, 1960, 469.
[9] Fischer, Öfele, Essler, Fröhlich, Mortenson, and Semmlinger, *Z. Naturforsch.*, 1958, **13b**, 458.

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Ring Contraction of Tritium-labelled Tropylium Complex (I).—(a) *Labelling of tricarbonylcycloheptatrienechromium.* In an apparatus similar to that described by Rydberg and Hanngren,[10] tricarbonylcycloheptatrienechromium (0·1 g.) was exposed to tritium (1 c) for 8 days. The labelled sample was diluted with inactive material (4 g.) and purified to constant count by subjecting it, in turn, seven times to chromatography on alumina, vacuum-sublimation, and recrystallisation from ligroin, benzene, or ether.

(b) *Assay* (method of Banks *et al.*[11]). The samples to be assayed (10 mg.) were rendered electrical conductors by grinding them with an equal weight of graphite in an agate mortar. In the case of the perchlorate, mixing and gentle pressing on filter paper had to be employed to avoid explosion. The mixture was pressed on a recessed nickel planchet with the end of a cylindrical metal rod. The activity was recorded in counts per minute (c.p.m.) as the average of six counts taken on this planchet in a windowless, flow-type Geiger counter with argon–methane as the carrier gas.

(c) *Reactions.* By the methods described above, tritium-labelled tricarbonylcycloheptatrienechromium (1·27 g.; 1080 c.p.m.) afforded active tricarbonyltropyliumchromium perchlorate (1·8 g.) which reached constant count (728 c.p.m.) after three crystallisations from acetone (Calc. count, equivalent labelling of all protons: 660 c.p.m.; calc. count, no labelling of methylene protons: 754 c.p.m.). This salt (1 g.) with an excess of cyclopentadienylsodium afforded tricarbonylbenzenechromium (0·288 g., 43%) which reached its constant count (980 c.p.m.) after four cycles of purification by sublimation, chromatography, and recrystallisation. This count is well within the expected limits of error (5%) of the value (952 c.p.m.) calculated on the assumption that the benzene residue is derived entirely from the tropylium group.

Reaction of Tricarbonyltropyliumchromium Perchlorate with Diethyl Sodiomalonate.—Diethyl malonate (1·28 g., 0·008 mole) was added to sodium ethoxide (0·006 mole) [from sodium (0·138 g., 0·006 g.-atom) and ethyl alcohol (5 ml.)] and the mixture stirred for 30 min. Tetrahydrofuran (20 ml.) and the perchlorate (I) (1·5 g., 0·0046 mole) were then added and the mixture was stirred overnight. The solvent was distilled off *in vacuo* and the red residue extracted with ligroin. Evaporation of the extract to dryness yielded red crystals (0·81 g.), which were chromatographed on neutralised alumina (90 g.) to give two major bands, with traces of two others. Elution with ligroin gave a trace of a red solid and also yellow needles of tricarbonylbenzenechromium (0·236 g., 24%), m. p. 162—163°, identified by mixed m. p. and infrared comparison with an authentic specimen. Ligroin–benzene (1 : 1) eluted *tricarbonyl(diethoxycarbonylmethylcycloheptatriene)chromium* (III; R = H) (0·552 g., 31%), crystallising from ligroin as orange-red plates, m. p. 122—123°, soluble in the common organic solvents (Found: C, 51·8; H, 4·8. $C_{17}H_{18}CrO_7$ requires C, 52·8; H, 4·7%).

Elution with benzene gave a small amount of a green gum (11 mg.), which had no infrared absorption in the carbonyl region and was not examined further.

Rearrangement of Tricarbonyl(diethoxycarbonylmethylcycloheptatriene)chromium (III; R = H).—(*a*) Tricarbonyl(diethoxycarbonylmethylcycloheptatriene)chromium (0·181 g., 0·00047 mole) and diethyl sodiomalonate (0·0033 mole) [from sodium metal (0·076 g., 0·0033 g.-atom) in ethanol (15 ml.) and diethyl malonate (1 g., 0·0062 mole)] were allowed to react at room temperature overnight. The solvent was then distilled *in vacuo* and the orange residue extracted with ligroin. Chromatography of the extract on alumina (50 g.) and elution with ligroin gave tricarbonylbenzenechromium (38 mg., 38%), m. p. 162—163°, identified by mixed m. p. and infrared comparison. Elution with benzene gave unchanged tricarbonyl(diethoxycarbonylmethylcycloheptatriene)chromium (7 mg.) as red plates, m. p. and mixed m. p. 122—123°.

(*b*) In a similar experiment, the malonate complex (III; R = H) (0·2 g.) was treated with sodium methoxide (from 0·2 g. of sodium and 10 ml. of methanol) and afforded tricarbonylbenzenechromium (47 mg., 42%).

Attempted Rearrangement of Tricarbonyl-7-[1,1-di(ethoxycarbonyl)ethyl]cycloheptatrienechromium (III; R = Me) *with Diethyl Sodiomalonate.*—The methylmalonyl complex [1] (III; R = Me) (0·4 g.) was recovered unchanged (0·375 g., 94%) when subjected to the reaction conditions (*a*) of the preceding experiment. No tricarbonylbenzenechromium was detected on chromatography.

Reaction of Sodium Cyclopentadienide with an Excess of Tricarbonyltropyliumchromium

[10] Rydberg and Hanngren, *Acta Chem. Scand.*, 1958, **12**, 322.
[11] Banks, Crawhall, and Smyth, *Biochem. J.*, 1956, **64**, 411.

Perchlorate.—Sodium cyclopentadienide (0·2 mole) was prepared from sodium wire (4·6 g., 0·2 g.-atom) and cyclopentadiene (13·2 g., 0·2 mole) in tetrahydrofuran (100 ml.), and a portion (1·2 ml., *ca.* 0·002 mole) added to a suspension of the perchlorate (I) (1 g., 0·0031 mole) in tetrahydrofuran (25 ml.). The mixture was stirred at room temperature overnight. Filtration, followed by evaporation, yielded a red gum (0·33 g.), which was chromatographed in ligroin–benzene (9 : 1) on alumina (100 g.). Elution with the same solvents gave tricarbonylbenzenechromium (8 mg.), m. p. and mixed m. p. 162—163°, and an orange-red gum (0·27 g., 46%), which crystallised with difficulty from ligroin–ether, then having m. p. 108—114° (decomp.). This product is presumably a mixture of isomers of *tricarbonylcyclopentadienylcycloheptatrienechromium* (IV; R = H) (Found: C, 61·3; H, 4·2. $C_{15}H_{12}CrO_3$ requires C, 61·6; H, 4·1%).

Elution with ligroin–benzene (1 : 1) gave an orange gum (66 mg.) which failed to crystallise. The infrared spectrum showed a strong resemblance to that of the compound, m. p. 108—114° (decomp.).

Reaction of Cyclopentadienylcycloheptatriene with Chromium Hexacarbonyl.—Cyclopentadienylcycloheptatriene [4] (4·05 g., 0·026 mole) and chromium hexacarbonyl (6 g., 0·027 mole) were heated in refluxing ligroin (b. p. 100—120°; 30 ml.) for 12 hr. The solvent was then removed *in vacuo* and the residue chromatographed in ligroin–benzene (9 : 1) on alumina (100 g.). Elution with the same solvents gave a red gum (0·54 g., 7·1%), which was further purified by chromatography on alumina. The infrared spectrum was identical with that of tricarbonylcyclopentadienylcycloheptatrienechromium, m. p. 108—114° (decomp.), described in the preceding experiment. Elution with benzene yielded a second red gum (31 mg.), with strong absorption at 1980 and 1896 cm.$^{-1}$ in the metal–carbonyl stretching region (CCl_4 solution).

Reaction of Tricarbonylcyclopentadienylcycloheptatrienechromium (IV; R = H) *with Sodium Methoxide.*—Sodium methoxide (0·01 mole) and tricarbonylcyclopentadienylcycloheptatrienechromium (200 mg., 0·00068 mole) [prepared from the tropylium complex (I)] in tetrahydrofuran (25 ml.) were stirred at room temperature for 12 hr. The solvent was then removed under reduced pressure and the residue extracted with ligroin. Chromatography on alumina (15 g.) and elution with ligroin gave tricarbonylbenzenechromium (36 mg., 24%) identified as before.

Attempted Rearrangement of Cyclopentadienylcycloheptatriene with Sodium Methoxide.—Cyclopentadienylcycloheptatriene [4] (1·56 g., 0·01 mole) was added to a solution of sodium methoxide [from sodium (2·3 g., 0·1 g.-atom) and methanol (50 ml.)] and stirred for 48 hr. at room temperature. Water (100 ml.) was then added and the mixture extracted with ether. No benzene was detected on vapour-phase chromatography of the washed and dried (Na_2SO_4) ether extract. . Evaporation of the solvent and infrared comparison of the residue (1·43 g.) with starting material showed that the product was unchanged.

Oxidation of Tricarbonyltropyliumchromium Perchlorate by Silver Oxide.—The perchlorate (0·65 g., 0·002 mole) in water (180 ml.) was stirred with silver oxide (0·7 g., 0·003 mole) overnight. The mixture was then extracted with ether, and the extract washed with water, dried ($MgSO_4$), and evaporated. Benzaldehyde was obtained (0·14 g., 67%) [2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 236—237°; infrared comparison (Found: C, 54·6; H, 3·5; N, 19·5. Calc. for $C_{13}H_{10}N_4O_4$: C, 54·5; H, 3·5; N, 19·6%)].

Reaction of Tricarbonyltropyliumchromium Perchlorate with Aqueous Hydrogen Peroxide.—The perchlorate (0·65 g., 0·002 mole) in water (200 ml.) at 5° was treated with 30% hydrogen peroxide (1 ml.) in water (5 ml.). Gas evolution took place and, after being stirred overnight, the mixture was extracted with ether. The pale yellow extract was washed with 10% aqueous sodium hydroxide (20 ml.), then water, and dried (Na_2SO_4). Evaporation gave a liquid (34 mg., 21·8%), b. p. 80°, having the same retention time as benzene on vapour-phase chromatography on a Griffin and George Mk2B apparatus, with 20% w/w " embaphase " silicone oil on " Celite-545 " as the stationary phase and nitrogen as the carrier gas.

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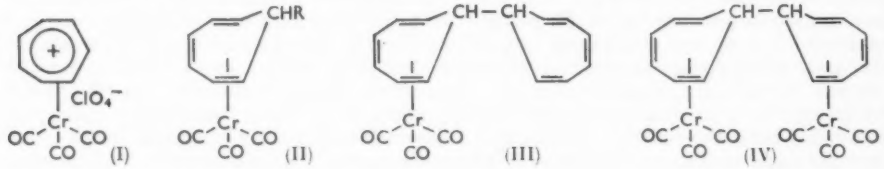
676. *Cycloheptatriene and Tropylium Metal Complexes. Part III.*[1] *The "Abnormal" Reaction with Anions.*

By J. D. Munro and P. L. Pauson.

Various anions are shown to cause reductive coupling of tricarbonyltropyliumchromium salts, giving a mixture of hexacarbonylbi(cycloheptadienyl)bischromium and tricarbonylbi(cycloheptadienyl)chromium as the principal products.

In Part I,[2] the normal reaction of the tricarbonyltropyliumchromium perchlorate (I) with anions was shown to be addition to the ring to produce compounds of the type (II). One of the first such reactions investigated by us was that with cyanide. Although the expected product (II; R = CN) was isolated in small amount, the two main products had compositions corresponding to the mono- (III) and bis-tricarbonylchromium derivative (IV) of



(I) (II) (III) (IV)

bi(cycloheptatrienyl). The structure of the latter was confirmed by its formation on reduction of the perchlorate (I) with zinc dust, and both products afforded bi(cylcoheptatrienyl) on treatment with diethylenetriamine. To test whether the alkalinity of cyanide solutions accounted for the formation of the dimeric products, the perchlorate (I) was treated with sodium hydrogen carbonate. The two bi(cycloheptatrienyl) derivatives (III and IV) were obtained in this way, and also by treating the tropylium compound (I) with sodium acetate, sodamide, phenyl-lithium, or benzamide.

We obtained the same products (III and IV) during an attempted acid hydrolysis of the malonate complex [1] [II; R = $CH(CO_2Et)_2$] and were thus led to treat the tropylium salt (I) with dilute hydrochloric acid. The formation of the bi(cycloheptatrienyl) derivatives (III and IV) under the latter conditions implies that the malonate complex [II; R = $CH(CO_2Et)_2$] is readily cleaved to give back diethyl malonate and the tropylium complex (I), a deduction which has been confirmed by subsequent work.[3] Similar cleavages of related metal-free cycloheptatriene derivatives have been observed and discussed by Conrow.[4]

We cannot propose a detailed mechanism for the coupling of tricarbonyltropyliumchromium salts by various anions to give bi(cycloheptatrienyl) derivatives, but the partial removal of chromium from the product is undoubtedly significant. In general terms it appears probable that attack by the anion on the chromium atom (in I or IV) leads to cleavage of the complex with liberation of a Cr(0) complex which then (like zinc) reduces the tropylium complex (I) to the bi(cycloheptatrienyl) complex (IV) by electron transfer.

Abel *et al.*[5] obtained a complex formulated as (III) by reaction of bi(cycloheptatrienyl) with chromium hexacarbonyl, but reported only the positions of its carbonyl stretching bands in the infrared. Repetition readily led to a crystalline product, but this differed from that (A) described above and is regarded as its stereo- (or possibly a position) isomer (B). No bischromium complex was isolated.

Reaction of the bischromium complex (IV) with triphenylmethyl perchlorate does not

[1] Part II, preceding paper.
[2] Munro and Pauson, *J.*, 1961, 3475.
[3] Pauson and Smith, unpublished observations.
[4] Conrow, *J. Amer. Chem. Soc.*, 1959, **81**, 5461.
[5] Abel, Bennett, Burton, and Wilkinson, *J.*, 1958, 4559.

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Vol. 1961, page 3484, line 3 of the summary. *For* (cycloheptadienyl) *read* (cycloheptatrienyl).

yield the corresponding cation (or the heptafulvalene complex which might be expected to result from proton elimination). Instead, cleavage to tricarbonyltropyliumchromium perchlorate (I) is observed.

Experimental

For general directions see Part I.[a]

Reaction of Tricarbonyltropyliumchromium Perchlorate with Potassium Cyanide.—(a) *In aqueous solution.* Solutions of the perchlorate (I) (0·756 g., 0·0023 mole) in water (150 ml.) and potassium cyanide (0·2 g., 0·0031 mole) in water (5 ml.) were mixed and left at room temperature for 10 min. The mixture was then extracted with ether, and the ether layer washed with water, dried (Na_2SO_4), and evaporated. The residue (0·42 g.) was chromatographed in ligroin–benzene (1 : 1) on alumina (150 g.), with the same solvents as eluent. Four bands were obtained yielding in order of elution: (1) Orange crystals of *tricarbonylbi(cycloheptatrienyl)chromium* (A) (III) (0·163 g., 46%), m. p. 148—149° (from ligroin) (Found: C, 63·9; H, 4·5; O, 14·9. $C_{17}H_{14}CrO_3$ requires C, 64·1; H, 4·4; O, 15·1%), soluble in the common organic solvents. (2) Deep red needles (86 mg., 17%) of *hexacarbonylbi(cycloheptatrienyl)bischromium* (IV), m. p. 223—225° (decomp.) (from benzene or acetone) alone or mixed with a specimen prepared by reduction of the perchlorate with zinc dust (see below) (Found: C, 52·8; H, 3·3; O, 20·8. $C_{20}H_{14}Cr_2O_6$ requires C, 52·9; H, 3·1; O, 21·1%), insoluble in ligroin and chloroform and only slightly soluble in ether and in tetrahydrofuran. (3) Yellow crystals (3·8 mg.) of unidentified structure [the compound forms yellow needles, m. p. 100—101°, from ligroin, is soluble in common organic solvents, and absorbs in the metal carbonyl stretching region of the infrared (KBr disc) at 1986, 1923, and 1892 cm.$^{-1}$ and in the C≡N stretching region at 2229 cm.$^{-1}$]. (4) Deep red needles of *tricarbonyl-7-cyanocyclohepta-1,3,5-trienechromium* (0·105 g., 18%), m. p. 118—119° (from ligroin–ether) (Found: C, 52·0; H, 3·0; N, 5·7. $C_{11}H_7CrNO_3$ requires C, 52·2; H, 2·8; N, 5·5%), soluble in benzene, ether, and ethanol, almost insoluble in ligroin or methylene chloride, having $\nu_{max.}$ in the C≡N stretching region at 2229 cm.$^{-1}$ (KBr disc).

(b) *In ethanol.* Tricarbonyltropyliumchromium perchlorate (1 g., 0·0031 mole) and potassium cyanide (0·5 g., 0·0077 mole) were refluxed in ethanol (30 ml.) for 1 hr. After evaporation under reduced pressure, the residue was extracted with ligroin and chromatographed on alumina (50 g.). Elution with ligroin gave tricarbonylbi(cycloheptatrienyl)chromium (A) (III) as orange needles (20 mg., 4·2%), m. p. and mixed m. p. 148—149°. The ligroin-insoluble material was dissolved in benzene and filtered from a mixture of unchange perchlorate and insoluble products (0·1 g.). The benzene-soluble fraction (0·46 g.) was chromatographed on alumina (60 g.) to yield hexacarbonylbi(cycloheptatrienyl)bischromium (IV) (0·28 g., 41·2%), yellow crystals (4 mg.) of the unidentified product, and tricarbonyl-7-cyanocyclohepta-1,3,5-trienechromium (97 mg., 12·8%), identity in each case being established by m. p., mixed m. p., and infrared comparison. In addition, a fifth band was eluted from the chromatogram. This afforded purple needles (3 mg.), which did not melt below 300°, are soluble in ether, acetone, and benzene and show carbonyl absorption at 1980 and 1900 cm.$^{-1}$ (KBr disc) but no C≡N absorption.

Repetition of this experiment with longer reaction times resulted in lower yields of tricarbonyl-7-cyanocyclohepta-1,3,5-trienechromium.

Other Reactions of the Perchlorate (I) *yielding the Bi(cycloheptatrienyl) Derivatives* (III *and* IV).—Reactions with the reagents listed in the Table were carried out similarly to that with

Reagent	Solvent	Reaction time [a] (hr.)	Products (III) mg.	(III) %	(IV) mg.	(IV) %
$NaHCO_3$ (excess)	Water	0·25	98	21	278	41
NaOAc (0·003 mole)	Methanol	1 [b]	130	29	280 [d]	41
$NaNH_2$ (0·006 mole)	Tetrahydrofuran	16	47	10	363	54
PhLi (0·005 mole)	Ether	16	57	12	233	33
Ph·CO·NH_2 (0·003 mole)	Water	6 [c]	110	23	305	45
HCl (excess, 2N)	Water	1 [b]	74	15	332	49

[a] At room temperature, unless otherwise indicated. [b] Under reflux. [c] At 80°. [d] Filtered off directly from the cooled mixture.

cyanide (above). The quantities are based on 1 g. (0·003 mole) of the perchlorate (I) in each case.

A third, unidentified substance (2·8 mg.), m. p. 124—129° (from ligroin), preceded the others

on chromatography of the product from the bicarbonate reaction. It showed metal–carbonyl absorption at 2000, 1934, and 1905 cm.$^{-1}$ (in CCl_4).

Reduction of Tricarbonyltropyliumchromium Perchlorate (I) *by Zinc Dust.*—The perchlorate (0·75 g., 0·0023 mole) in tetrahydrofuran (30 ml.) was shaken with zinc dust (0·4 g.) at room temperature for 36 hr. The solvent was evaporated *in vacuo* and the residue extracted with benzene and chromatographed on alumina (55 g.). Elution with benzene gave hexacarbonylbi(cycloheptatrienyl)bischromium (IV) (0·3 g., 58%), which recrystallised from acetone as deep red needles, m. p. 223—225° (decomp.) (Found: C, 52·7; H, 3·3; O, 20·9. Calc. for $C_{20}H_{14}Cr_2O_6$: C, 52·9; H, 3·1; O, 21·1%), slightly soluble in ether and tetrahydrofuran and almost insoluble in ligroin.

Reaction of Bi(cycloheptatrienyl) with Chromium Hexacarbonyl.—Bi(cycloheptatrienyl) [6] (3·32 g., 0·018 mole) and chromium hexacarbonyl (8 g., 0·036 mole) were refluxed in ligroin (b. p. 100—120°, 50 ml.) for 24 hr. Filtration followed by evaporation *in vacuo* yielded a red gum, which was chromatographed on alumina (250 g.). Elution with ligroin afforded unchanged bi(cycloheptatrienyl) (0·81 g.), m. p. 69—70°, and a red gum (0·57 g.), which was rechromatographed on alumina and then partly crystallised from ligroin as red needles of *tricarbonylbi(cycloheptatrienyl)chromium* (B) (III) (53 mg.), m. p. 124—125° (Found: C, 64·2; H, 5·2. $C_{17}H_{14}CrO_3$ requires C, 64·1; H, 4·4%). Only uncrystallisable gums were obtained from the mother-liquors. The last compound is soluble in all common organic solvents and shows strong absorption at 1980, 1931 and 1873 cm.$^{-1}$ in the metal-carbonyl stretching frequency region. A trace of a second red band was eluted with light petroleum–benzene (1 : 1), but was obtained in too low a yield for characterisation.

Reactions of Bi(cycloheptatrienyl) Complexes with Diethylenetriamine.—Each of the three bi(cycloheptatrienyl) complexes [III (A), III (B), and IV] 100 mg.) was heated with diethylenetriamine (5 ml.) at 100° for 30 min. After addition of water (50 ml.) the mixtures were extracted with ether. In each case, evaporation of the ether layer afforded bi(cycloheptatrienyl), m. p. and mixed m. p. 69—70°, and filtration of the aqueous layer afforded tricarbonyldiethylenetriaminechromium,[7] both in 70—80% yield. The chromium complex darkened above 220° but did not melt below 300°, and proved insoluble in all common organic solvents (Found: C, 35·3; H, 5·6. Calc. for $C_7H_{13}CrN_3O_3$: C, 35·2; H, 5·4%).

Reaction of Hexacarbonylbi(cycloheptatrienyl)bischromium with Triphenylmethyl Perchlorate.—Triphenylmethyl perchlorate (0·342 g., 0·001 mole) in methylene chloride (10 ml.) was added to hexacarbonylbi(cycloheptatrienyl)bischromium (IV) (0·454 g., 0·001 mole) in the same solvent (50 ml.). Tricarbonyltropyliumchromium perchlorate (I) (0·24 g.) was precipitated and was characterised by reduction with sodium borohydride and with zinc dust to tricarbonylcycloheptatrienechromium (II; R = H) and hexacarbonylbi(cycloheptatrienyl)bischromium (IV) respectively, the identities being confirmed by mixed m. p.s and infrared comparisons. The tri-iodide was also prepared and crystallised from acetone as brown needles, decomp. >150° (Found: C, 19·8; H, 1·1. Calc. for $C_{10}H_7CrI_3O_3$: C, 19·7; H, 1·2%), having the correct infrared spectrum.

Acid Hydrolysis of Tricarbonyl-7-[1,1-di(ethoxycarbonyl)ethyl]cycloheptatrienechromium [II; R = $CMe(CO_2Et)_2$].—The methylmalonyl complex [2] (0·25 g., 0·00063 mole) was heated with 20% hydrochloric acid (3 ml.) for 1 hr. at 100°. The mixture was poured into water (20 ml.) and extracted with ether (2 × 250 ml.). Evaporation of the washed and dried (Na_2SO_4) ether extract gave red crystals (157 mg.), which were triturated with ligroin and chromatographed on neutralised alumina (30 g.), to give two bands. Elution wth ligroin yielded tricarbonylbi(cycloheptatrienyl)chromium (A) (III) (3·1 mg.) as orange needles, m. p. and mixed m. p. 148—149°. Elution with benzene gave starting material (29 mg.), m. p. 91—92°. The ligroin-insoluble material was chromatographed in benzene on alumina (45 g.), giving a single red band. Elution with benzene yielded hexacarbonylbi(cycloheptatrienyl)bischromium (51 mg., 36%), identified by m. p., mixed m. p., and infrared comparison.

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[6] Doering and Knox, *J. Amer. Chem. Soc.*, 1954, **76**, 3203.
[7] Abel, Bennett, and Wilkinson, *J.*, 1959, 2323.

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677. *Reactions at Position* 1 *of Carbohydrates. Part I. The Polarographic Reduction of Carbohydrates.*

By W. G. Overend, A. R. Peacocke, and J. B. Smith.

An investigation has been made of the polarography of a variety of sugars and their derivatives in a buffer solution based on the tetramethylammonium ion. Reasonable polarographic waves were obtained with limiting currents proportional to sugar concentration over a wide range. For unsubstituted sugars the limiting current was independent of the mercury-reservoir height and so was determined by the rate of transformation of the αβ-equilibrium mixture of the sugar from ring to reducible form at the mercury surface, and not by the rate of diffusion of the sugar to the mercury drop. With some methylated pentose derivatives diffusion became the rate-controlling step.

In 1932, Heyrovsky and Smoler [1] reported that glucose and several other simple sugars were not reduced at the dropping-mercury electrode, a conclusion which was revised when Cantor and Peniston [2] obtained polarographic waves for various aldoses. Relatively high concentrations (*ca.* 0·1M) were required and the limiting currents observed were low. This was explained by suggesting that the *aldehydo*-form of the sugar was in equilibrium with a much larger amount of the ring form and that the *aldehydo*-form alone was reducible so that only low limiting currents, controlled by the rate of diffusion of this form to the drop surface, could be expected. This interpretation was disproved by Wiesner [3] who obtained polarographic waves for several aldoses and demonstrated that the heights of such waves were independent of the head of mercury above the drop. Wiesner accordingly concluded that the limiting current was determined, not by the rate of diffusion of the *aldehydo*-form to the mercury drop, but by the rate of transformation of the αβ-equilibrium mixture from the ring to the open-chain reducible form at the surface of the mercury drop. Further, he showed that the equilibrium concentration of the *aldehydo*-form was negligible. In view of the proposal that the limiting current was determined by the rate of transformation of the ring-form to the open-chain form of the sugar, it was decided to investigate the effect, on this rate, of factors which are likely to alter the stability of the ring-form relative to that of the open-chain structure.

The polarography of a variety of sugars and their derivatives was investigated, the buffer solution being based on the tetramethylammonium ion. This solution consisted of a mixture of tetramethylammonium phosphate and phosphoric acid at pH 8·0 and gave a constant concentration of 0·002M-tetramethylammonium ion in the polarographic test solution. The advantage of using this buffer lies in the high decomposition potential of the tetramethylammonium ion (about −2·5 v). The half-wave potentials of 2-deoxy-sugars were found to be in the region −2·1 to −2·2 v, and only in this buffer solution did these sugars give discrete waves amenable to measurement. It was essential to remove all traces of alkali-metal ions from the sugars, since the reduction waves of these ions otherwise overlapped and obscured those of the sugars themselves.

A preliminary account of some of this work was published recently.[4]

Results

The sugars were found to give reproducible polarographic waves in the tetramethylammonium phosphate buffer solution, and representative curves are shown in Figs. 1, 2, and 3. For all except two of the sugars studied, the limiting current generated by the sugar was independent

[1] Heyrovsky and Smoler, *Coll. Czech. Chem. Comm.*, 1932, **4**, 521.
[2] Cantor and Peniston, *J. Amer. Chem. Soc.*, 1940, **62**, 2113.
[3] Wiesner, *Coll. Czech. Chem. Comm.*, 1947, **12**, 64.
[4] Overend, Peacocke, and Smith, *Chem. and Ind.*, 1957, 113, 1383.

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of the mercury-reservoir height. This result, first observed by Wiesner,[3] shows that the rate of polarographic reduction is not determined by the rate of diffusion to the mercury drop, but by the rate of transformation of the αβ-equilibrium mixture from ring to reducible form at the mercury surface. The two exceptional compounds, 2,3,4-tri-*O*-methyl-L-arabopyranose and 2,3,5-tri-*O*-methyl-D-ribofuranose generated limiting currents which were accurately proportional to the square root of the head of mercury. This result, which is illustrated in Table 1, shows that for these two compounds the rate of transformation from ring to reducible form is sufficiently high to render diffusion to the mercury drop surface the slowest, rate-controlling step.

FIGS. 1—3. *Polarographic waves in* 0·002M-*tetramethylammonium phosphate buffer* (pH 8·0) *at* 25° *at various heights of the mercury reservoir (see below). The scale of applied voltage on the abscissa is moved to the right by* 0·4 V *for each successive curve, reading from left to right.*

FIG. 1. FIG. 3.

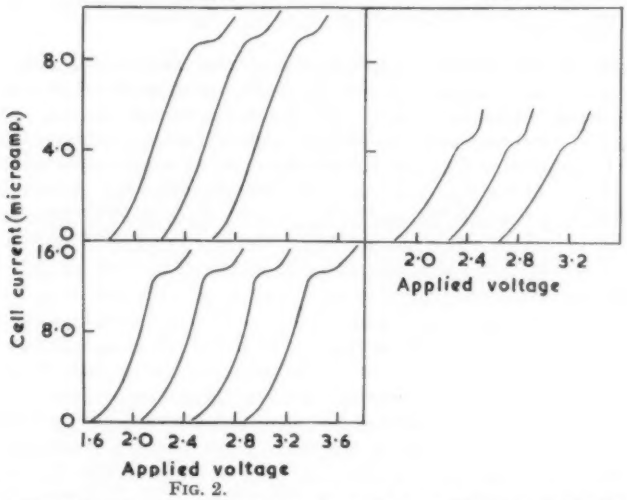

FIG. 2.

FIG. 1. D-Ribose (0·008M). Reservoir heights (from left to right): 45·5, 38·2, 30·8 cm.
FIG. 2. 2-Deoxy-D-galactose (0·008M). Reservoir heights (from left to right): 51·6, 48·0, 45·2, 41·4 cm.
FIG. 3. 2-Deoxy-D-ribose (0·008M). Reservoir heights (from left to right): 44·2, 41·2, 34·9 cm.

TABLE 1. *Relation between limiting current and mercury head at* 25°.

2,3,4-*Tri*-O-*methyl*-L-*arabopyranose* (0·002M; pH 8·0; 25°)						
Mercury head (*H*) (mm.)	534	498	458	421	382	351
Limiting current (*i*) (microamp.)	6·3	6·0	5·8	5·5	5·2	5·0
$H^{\frac{1}{2}}/i$	3·7	3·7	3·7	3·7	3·7	3·7
2,3,5-*Tri*-O-*methyl*-D-*ribofuranose* (0·043M; pH 8·0; 25°)						
Mercury head (*H*) (mm.)	430	389	338	295	248	
Limiting current (*i*) (microamp.)	14·8	14·0	13·0	12·1	11·1	
$H^{\frac{1}{2}}/i$	1·4	1·4	1·4	1·4	1·4	

In order to provide a standard scale of reference, all half-wave potentials were measured relatively to the saturated calomel electrode. The results appear in Table 2. The half-wave potentials of the 2-deoxy-sugars lie in the range −2·1 to −2·18 V, whereas those of the normal sugars vary from −1·87 to −2·12 V. It is particularly noticeable that 2,3,4-tri-*O*-methyl-L-arabopyranose and 2,3,5-tri-*O*-methyl-D-ribofuranose, which both generate diffusion-controlled waves, exhibit more positive half-wave potentials (−1·36 and −1·57 V, respectively) than all of the other sugars studied. The half-wave potentials were independent of sugar concentation and became more negative when the pH of the solution was increased.

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Effect of Sugar Concentration on Limiting Current.—Ideally, the limiting current should be directly proportional to the sugar concentration, and this relation has been found to apply over limited ranges of concentration for all compounds examined. At high sugar concentrations deviations from proportionality occur as exemplified by curve C in Fig. 4 for D-ribose, and have been observed also with D-galactose, 2-deoxy-D-galactose, and 3,5,6-tri-*O*-methyl-D-glucofuranose. This decrease in the ratio of limiting current to concentration which occurs at high concentrations (*ca.* 0·1M) may be the result either of a change from a first-order to a more complex reaction or to an increase in viscosity, causing a decrease in the diffusion coefficient to the point where it determines the rate of polarographic reduction. A decrease in the value of the diffusion coefficient would cause a corresponding decrease in the limiting current, in accordance with Ilkovic's equation [5] for diffusion-controlled polarographic reduction. Friedman and Carpenter [6] have shown that the diffusion coefficient of D-glucose at 25° is a linear function of the square root of the sugar concentration, so that deviations from strict proportionality between limiting current and concentration are possible over wide ranges of concentration.

Determination of Rate Constants.—A quantity A, the limiting current generated per unit concentration, was obtained from the linear section of the current–concentration graph for each sugar, and these A values are shown in Table 2. There are two treatments which relate the ratio A to the rate constants for the transformation of the αβ-equilibrium mixture from ring to reducible form:

(i) Delahay [7] considered the reduction of the αβ equilibrium mixture, and assumed the reaction scheme $\alpha\beta \underset{}{\overset{k_f^{\alpha\beta}}{\rightleftharpoons}} \gamma$, where γ represents the reducible intermediate, presumably the *aldehydo*-form. The overall equilibrium constant K for the reaction is equal to $[\gamma]/[\alpha\beta]$. The limiting kinetic current, i (microamp.), is then shown to be given by the equations:

$$i = 0{\cdot}6Pn(m\tau)^{2/3}ck_s^{\alpha\beta} \qquad (1)$$

and

$$i = 0{\cdot}6Pn(m\tau)^{2/3}c(DKk_f^{\alpha\beta})^{1/2} \qquad (2)\ (A = i/c)$$

In these equations, P is a constant equal to 1255 at 25°, n is the number of electrons required for the reduction of one sugar molecule (a value $n = 2$ is consistent with the reduction mechanism proposed), m is the mercury flow rate in mg. sec.$^{-1}$, τ is the mercury drop time in seconds, c is the sugar concentration in millimoles litre^{-1}, and D is the sugar diffusion coefficient in cm.^{2} sec.$^{-1}$: $k_s^{\alpha\beta}$ and $k_f^{\alpha\beta}$ are, respectively, the heterogeneous and the homogeneous rate constants for the transformation from cyclic to reducible form, and K is the overall equilibrium constant of the transformation as already defined. The value of $k_s^{\alpha\beta}$ is expressed in cm. sec.$^{-1}$ and that of $k_f^{\alpha\beta}$ in sec.$^{-1}$, and Delahay related these constants by assuming that the transformation reaction occurs essentially in a " monolayer " at the surface of the mercury drop. Then $k_f^{\alpha\beta} = k_s^{\alpha\beta}/\delta$ where δ is the thickness (in cm.) of a " monolayer " of the sugar ring form, and this thickness was arbitrarily assumed [7] to equal the mean distance between two sugar molecules in solution. Equations (1) and (2) may be compared, showing that

$$K = (k_s^{\alpha\beta})^2/Dk_f^{\alpha\beta}, \qquad (3)$$

so that if D, the sugar diffusion coefficient is known, the rate and equilibrium constants may be calculated from experimentally determined quantities. The values of $k_s^{\alpha\beta}$, $k_f^{\alpha\beta}$, and K for the sugars studied are shown in Table 2 and have a reproducibility of 5—7%.

(ii) In a polarographic study on the mutarotation of D-glucose, Los, Simpson, and Wiesner [8] adopted the reaction scheme $\alpha \underset{k_b^{\alpha}}{\overset{k_f^{\alpha}}{\rightleftharpoons}} \gamma \underset{k_f^{\beta}}{\overset{k_b^{\beta}}{\rightleftharpoons}} \beta$, where γ again represents the reducible intermediate. (This formulation involves the rate constants for the equilibrium $\alpha \rightleftharpoons \beta$, so these need not be further specified.) From the equations derived by these workers, it can be shown that the limiting current i $(= Ac)$ is given by the relation:

$$i = Gn(m\tau)^{2/3}D^{1/2}\frac{(k_f^{\alpha}c_{\alpha} + k_f^{\beta}c_{\beta})}{(k_b^{\alpha} + k_b^{\beta})^{1/2}}, \qquad (4)$$

[5] Ilkovic, *Coll. Czech. Chem. Comm.*, 1934, **6**, 498.
[6] Friedman and Carpenter, *J. Amer. Chem. Soc.*, 1939, **61**, 1745.
[7] Delahay, *J. Amer. Chem. Soc.*, 1951, **73**, 4944; 1952, **74**, 3506.
[8] Los, Simpson, and Wiesner, *J. Amer. Chem. Soc.*, 1956, **78**, 1564.

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in which G is a constant equal to 493 at 25°, c_α and c_β are respectively the concentrations in millimoles l.$^{-1}$ of the α- and the β-anomer at mutarotation equilibrium, the rate constants are expressed in sec.$^{-1}$, and other factors have their previous significance. Thus, the experimental quantity $A = i/c = i/(c_\alpha + c_\beta)$ depends on the ratio of quantities involving the first powers of k_f^α and k_f^β to $(k_b^\alpha + k_b^\beta)^{1/2}$, and this fuller analysis shows the limitations of Delahay's treatment which ignores differences between the rates of the back reactions $\gamma \longrightarrow \alpha$ and $\gamma \longrightarrow \beta$. However, if $k_f^\alpha = k_f^\beta = k_f^{\alpha\beta}$, and $k_b^\alpha = k_b^\beta = k_b^{\alpha\beta}$, equation (4) reduces to

$$i = Gn(m\tau)^{2/3}D^{1/2}c\frac{\sqrt{2}\,.\,k_f^{\alpha\beta}}{(k_b^{\alpha\beta})^{1/2}} \qquad (5)$$

or

$$i = Gn(m\tau)^{2/3}D^{1/2}cB, \qquad (5a)$$

where B is the ratio $\sqrt{2}\,.\,k_f^{\alpha\beta}/(k_b^{\alpha\beta})^{\frac{1}{2}}$. The value of B will increase with increase in the rate of the forward reaction ($\alpha\beta \longrightarrow \gamma$) and with decrease in that of the back-reaction ($\gamma \longrightarrow \alpha\beta$). Thus the ratio B provides a measure of the ease of transformation from cyclic to reducible form which is appropriately weighted to allow for the rate of the back-reaction, and accordingly represents a quantity more valuable and informative for carbohydrate reactivity studies than does the supposed $k_f^{\alpha\beta}$ derived from Delahay's analysis. In Table 2 the sugars studied are

TABLE 2. *General properties of the polarographic waves of sugars at* pH 8·0 *and* 25° *in* 0·002M-*tetramethylammonium phosphate buffer.*

Sugar or sugar derivative	Mercury head dependence	$E_{\frac{1}{2}}$ (S.C.E.) (v)	A (microamp. l. mmole^{-1})	$10^5 k_s^{\alpha\beta}$ (cm. sec.$^{-1}$)	$k_f^{\alpha\beta}$ (sec.$^{-1}$)	$10^3 K$	B (sec.$^{-\frac{1}{2}}$)
2,3,4-Tri-*O*-methyl-L-arabopyranose	$\propto H^{\frac{1}{2}}$	−1·36	2·5	>1300			
2,3,5-Tri-*O*-methyl-D-ribofuranose	$\propto H^{\frac{1}{2}}$	−1·57	0·4	>1300			
2-Deoxy-L-ribose	$\propto H^0$	−2·10	1·9	63	890	6600	0·37
2-Deoxy-D-ribose	,,	−2·10	1·9	62	880	6500	0·37
D-Ribose	,,	−2·03	1·2	36	600	3200	0·22
2-Deoxy-D-allose	,,	−2·16	0·61	23	530	1500	0·14
2-Deoxy-D-galactose	,,	−2·13	0·68	25	260	3500	0·14
3,5,6-Tri-*O*-methyl-D-glucofuranose	,,	−1·91	0·28	8·5	87	1200	0·050
2-Deoxy-D-glucose	,,	−2·18	0·20	7·6	180	500	0·045
3-Deoxy-D-allose	,,	−2·03	0·14	5·0	130	300	0·029
L-Arabinose	,,	−2·12	0·14	4·7	80	410	0·028
2,3,4-Tri-*O*-methyl-D-ribopyranose	,,	−2·21	0·10	3·4	98	180	0·020
D-Lyxose	,,	−1·93	0·088	2·2	80	89	0·013
D-Xylose	,,	−2·05	0·071	2·1	35	180	0·012
D-Galactose	,,	−1·97	0·040	1·3	38	68	0·0078
2-*O*-Methyl-L-arabinose	,,	−1·71	0·036	0·96	37	37	0·0057
D-Mannose	,,	−1·91	0·033	0·90	33	37	0·0051
D-Glucose	,,	−1·87	0·01	0·27	13	9·0	0·0017
3-*O*-Methyl-D-glucose	,,	−1·73	0·004	0·10	2·5	6·6	0·00063
2,3,4,6-Tetra-*O*-methyl-D-glucopyranose			≪0·1	≪1			≪0·1

arranged in order of B values. The sugar diffusion coefficient (D) was assumed throughout to be $6{\cdot}7 \times 10^{-6}$ cm.^{2} sec.$^{-1}$, the value obtained by Friedman and Carpenter [6] for 0·1M-D-glucose at 25°.

From a comparison of equations (1) and (5*a*), the ratio B may be related to the rate constant $k_s^{\alpha\beta}$ of Delahay's treatment. Thus, $B = 0{\cdot}6Pk_s^{\alpha\beta}/GD^{\frac{1}{2}}$, and at 25° when $P = 1255$ and $G = 493$, $B = 1{\cdot}53k_s^{\alpha\beta}/D^{\frac{1}{2}} = 590k_s^{\alpha\beta}$ when the above value for D is used: hence B and k_s are directly proportional.

These equations show that a limiting current which is controlled by a reaction rate is dependent on the product $(m\tau)^{2/3}$, which is proportional to the surface area of the mercury drop. Since the area of the mercury drop is independent of the mercury-reservoir height, the magnitudes of limiting currents controlled by reaction rates show a similar independence. When the limiting current depends on a diffusion rate, the instantaneous current generated

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depends not only on the area of the drop, but also on a function of the mercury drop time. This arises because the amount of material diffusing to the mercury surface depends on these same two factors and the limiting current is proportional to $m^{2/3}\tau^{1/6}$, as in the Ilkovic equation.

When the rates of diffusion and reaction are joint controlling factors, the limiting current depends on a power of τ between 2/3 and 1/6. Thus, the magnitude of a limiting current which is controlled to any extent by diffusion should not be independent of the mercury reservoir height.

In the cases of 2,3,4-tri-*O*-methyl-L-arabopyranose and 2,3,5-tri-*O*-methyl-D-ribofuranose, the polarographic reduction was diffusion-controlled, so that the rate constants for the transformation from cyclic to reducible form could not be calculated on the basis of the above two treatments. Nevertheless, lower limiting values of $k_s^{\alpha\beta}$ were available since Delahay showed that for a diffusion-controlled reduction of this type, the product $k_s^{\alpha\beta}D^{-1/2}$ must exceed five. This result does not depend on the assumptions involving the reaction layer thickness " δ," and lower limiting values of $k_s^{\alpha\beta}$ for these two methylated sugars are shown in Table 2.

Effect of Temperature Variation.—(a) *2,3,4-Tri-O-methyl-L-arabopyranose and 2,3,5-tri-O-methyl-D-ribofuranose.* Even in the region of 0°, the limiting currents generated by these compounds remained accurately proportional to the square root of the head of mercury (see Table 3). Evidently the rate of transformation to the reducible form is much faster for these

TABLE 3. *Relation between limiting current and mercury head at low temperatures.*

(*a*) 2,3,4-Tri-*O*-methyl-L-arabopyranose (0·005M; pH 8·0; 0·1°)					
Mercury head (H) (mm.)	480	420	390	360	320
Limiting current (i) (microamp.)	9·0	8·4	8·0	7·7	7·3
$H^{\frac{1}{2}}/i$	2·4	2·4	2·5	2·5	2·4
(*b*) 2,3,5-Tri-*O*-methyl-D-ribofuranose (0·043M; pH 8·0; 1·1°)					
Mercury head (H) (mm.)	449	419	379	339	299
Limiting current (i) (microamp.)	9·9	9·6	9·1	8·8	8·1
$H^{\frac{1}{2}}/i$	0·68	0·67	0·68	0·67	0·68

compounds than for the other sugars studied. The approximate temperature coefficients of limiting current in the region of 25° were +2·3% per degree for 2,3,4-tri-*O*-methyl-L-arabopyranose, and +1·7% per degree for 2,3,5-tri-*O*-methyl-D-ribofuranose. These figures are typical of a diffusion-controlled reduction (the temperature coefficients of diffusion current for many common ions range from +1·3 to +2·3% per degree [9]).

(b) *D-Ribose and 2-deoxy-D-ribose.* The variation with temperature of the values of A and B was studied for these two sugars. A and B are related by equation (5*a*) in which the constant G is equal to 493 at 25°, and at other temperatures this value must be corrected (it has a very small temperature coefficient [10] of +0·00012 deg.$^{-1}$).

By using equation (5*a*) with the appropriately corrected G value, the ratios A and B were determined for D-ribose and 2-deoxy-D-ribose at various temperatures between 0° and 60°, and log B was plotted against the reciprocal of the absolute temperature (Fig. 5). Since B is directly proportional to the " heterogeneous " rate constant of the transformation from cyclic to reducible form (Delahay's $k_s^{\alpha\beta}$), the gradient of the plot in Fig. 5 may be regarded as a measure of the activation energy involved in electroreduction. Above about 30°, these plots deviate markedly from linearity, and this may arise for two reasons. First, the rate of transformation from ring to reducible form may have increased to such an extent that diffusion is becoming a rate-controlling factor: the temperature coefficients of A (and hence of B) for D-ribose and 2-deoxy-D-ribose would then decrease from a value of +10% per degree shown by both sugars in the region of 20°, and approach the value of +2% per degree, which is characteristic of the two tri-*O*-methyl sugars generating diffusion-controlled limiting currents. Secondly, at higher temperatures the reduction may proceed by an alternative mechanism of lower overall activation energy.

The activation energies involved in the polarographic reduction of D-ribose and 2-deoxy-D-ribose were calculated from the gradients of the linear sections of Fig. 5 as 25 and 23 kcal./mole, respectively. These activation energies are greater than the value of

[9] Nejedly, *Coll. Czech. Chem. Comm.*, 1929, **1**, 319.
[10] Cf. Kolthoff and Lingane, " Polarography," Interscience Publ. Inc., New York, 1952, 2nd edn., Vol. I, Chap. 4.

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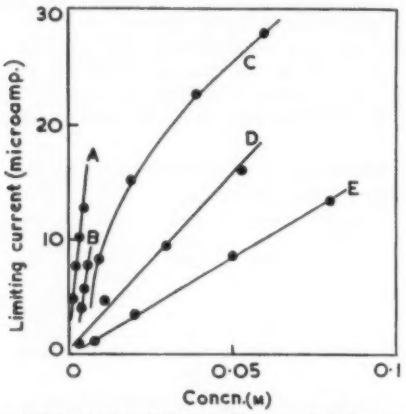
16·5 kcal./mole obtained by Delahay and Strassner [11] for the reduction of L-arabinose, D-xylose, D-galactose, D-mannose, and D-glucose at pH 7·75. However, the results obtained by these workers are not readily interpreted since they used highly concentrated (0·5M) sugar solutions; they would exhibit too low a ratio of limiting current to concentration (*A* value) for under these conditions the current–concentration curves are not linear (Fig. 4).

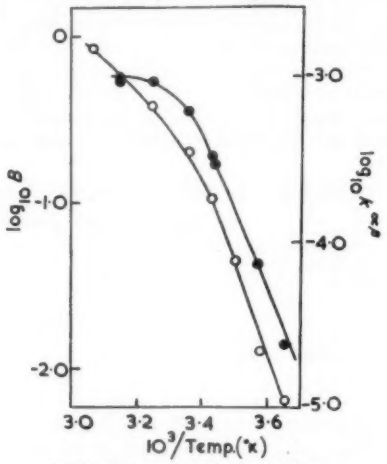
Effect of pH *Variation.*—(a) 2,3,4-*Tri*-O-*methyl*-L-*arabopyranose and* 2,3,5-*tri*-O-*methyl*-D-*ribofuranose.* Variation of pH over a wide range had no significant effect on the *A* value for either of these compounds (Table 4). This accords with the view that these compounds generate

FIG. 4. *The effect of sugar concentration on the limiting polarographic current in* 0·002M-*tetramethylammonium phosphate buffer* (pH 8·0) *at* 25°.



A, 2,3,4-Tri-*O*-methyl-L-arabinose; *B*, 2-deoxy-D-ribose; C, D-ribose; D, 2,3,5-tri-*O*-methyl-D-ribose; E, 2-deoxy-D-glucose.

FIG. 5. *Dependence of the quantities B and* $k\alpha\beta$ *on temperature at* pH 8·0.



○ D-Ribose; ● 2-deoxy-D-ribose.

limiting currents which are determined by the rate of diffusion to the mercury drop surface since this rate does not depend on pH.

TABLE 4. *Variation of A values with* pH *at* 25°.

(*a*) 2,3,4-Tri-*O*-methyl-L-arabopyranose

pH	3·30	4·98	6·25	7·48
A (microamp. mmole $l.^{-1}$)	2·11	2·14	2·19	2·14

(*b*) 2,3,5-Tri-*O*-methyl-D-ribofuranose

pH	3·18	3·98	5·79	7·24
A (microamp. mmole $l.^{-1}$)	0·23	0·22	0·22	0·23

(b) D-*Ribose and* 2-*deoxy*-L-*ribose.* Variation in pH was found to have a marked effect on the values of *A* and *B* for these sugars (Table 5). The results obtained for D-ribose indicate that the transformation of the αβ-equilibrium mixture from ring to reducible form is catalysed by hydrogen and hydroxyl ions with a minimum velocity at pH 3·5—6. The values of the catalytic constants for the reduction of D-ribose were: $k_{H^+} = 9{\cdot}9 \times 10^3$ l. $mole^{-1}$ $sec.^{-1}$, $k_{OH^-} = 1{\cdot}6 \times 10^6$ l. $mole^{-1}$ $sec.^{-1}$ and $k_{OH^-}/k_{H^+} = 162$ at 25°. (The constants k_{H^+} and k_{OH^-}, when multiplied by the concentration of hydrogen or hydroxyl ion respectively, represent the contribution of these catalytic effects to the rate constants of the forward reaction.) These results are in accordance with the work of Delahay and Strassner who showed that increase in pH increased the limiting currents of several simple sugars. These workers did not study the pH effect below pH 6·5, and so did not observe hydrogen-ion catalysis, although Cantor and

[11] Delahay and Strassner, *J. Amer. Chem. Soc.*, 1952, **74**, 893.

Peniston reported hydrogen-ion catalysis in the reduction of D-ribose and L-allose and suggested that the effect might be general.

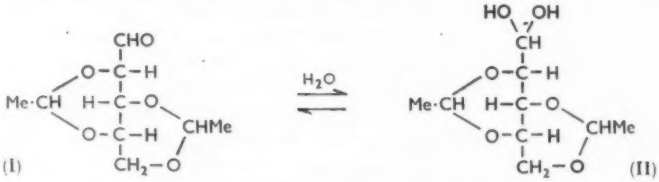
TABLE 5. *Variation of A and B values with* pH *at* 25°.

(*a*) D-Ribose				(*b*) 2-Deoxy-L-ribose			
pH	*A* (microamp. mmole $l.^{-1}$)	*B* ($sec.^{-1/2}$)	$10^4 . k_s\alpha\beta$ ($cm. sec.^{-1}$)	pH	*A* (microamp. mmole $l.^{-1}$)	*B* ($sec.^{-1/2}$)	$10^4 . k_s\alpha\beta$ ($cm. sec.^{-1}$)
1·76	0·50	0·067	1·13	4·42	$\leqslant 1$	—	—
2·66	0·51	0·039	0·66	5·92	0·18	0·030	0·51
3·51	0·097	0·0077	0·13	8·34	0·15	0·24	4·12
4·20	0·11	0·017	0·285	10·48	0·17	0·28	4·71
6·00	0·14	0·023	0·385				
7·22	0·56	0·089	1·51				
8·72	0·93	0·15	2·47				
9·90	1·2	0·19	3·16				

Polarography of 2,4:3,5-*Di*-O-*ethylidene*-aldehydo-L-*xylose*.—With this compound in the usual 0·002M-tetramethylammonium phosphate–phosphoric acid mixture fluctuating non-reproducible waves were obtained and this was attributed to failure to maintain steady pH conditions in the region of the mercury drop surface. Accordingly further work was conducted with 0·01M-sodium borate buffer (pH 9·18) which has a much higher buffering capacity than the 0·002M-tetramethylammonium solution. In the borate medium the *aldehydo*-sugar generated clear reproducible waves (half-wave potential = −1·42 v) with limiting currents proportional to sugar concentration over a wide range. The limiting current was independent of the mercury head, indicating that the reduction rate was controlled by the rate of transformation of the *aldehydo*-sugar from a non-reducible to a reducible form at the mercury drop surface.

This behaviour may be compared with the polarography of simple aldehydes. Veseley and Brdicka [12] have shown that formaldehyde gives kinetic limiting currents determined by the acid–base-catalysed dehydration rate of the hydrated methylene glycol structure: $H_2C(OH)_2 \rightleftharpoons H_2C{=}O + H_2O$. Acetaldehyde [13] and propionaldehyde [14] give reduction waves which are less dependent on temperature and pH since these aldehydes are less hydrated than formaldehyde. Their limiting currents are controlled partly by diffusion and partly by the rate of dehydration of the hydrated structure. The dehydration of acetaldehyde hydrate has been studied extensively [15] and has been shown to undergo general acid–base catalysis.[16]

In common with other *aldehydo*-sugars,[17] 2,4:3,5-di-*O*-ethylidene-*aldehydo*-L-xylose (I) has been shown [18] to react instantaneously with water to give the hydrated form (II). It seems



probable, therefore, that the rate of polarographic reduction of the *aldehydo*-sugar is controlled exclusively by the dehydration rate of the non-reducible form (as II). Acid–base catalysis of the reduction may then be interpreted in terms of a mechanism of the type proposed by Bell and Higginson [16] for acetaldehyde hydrate.

[12] Veseley and Brdicka, *Coll. Czech. Chem. Comm.*, 1947, **12**, 313.
[13] Bieber and Trumpier, *Helv. Chim. Acta*, 1947, **30**, 2000.
[14] Bieber and Trumpier, *Helv. Chim. Acta*, 1948, **31**, 5.
[15] Herold and Wolf, *Z. phys. Chem.*, 1931, *B*, **12**, 165; Herbert and Lander, *Trans. Faraday Soc.*, 1938, **34**, 432, 1219.
[16] Bell and Higginson, *Proc. Roy. Soc.*, 1949, *A*, **197**, 141; Bell and Darwent, *Trans. Faraday Soc.*, 1950, **46**, 34.
[17] Levene and Meyer, *J. Biol. Chem.*, 1927, **74**, 695; Wolfrom, *J. Amer. Chem. Soc.*, 1931, **53**, 2275; Hann, Ness, and Hudson, *ibid.*, 1944, **66**, 665; Stacey and Turton, *J.*, 1946, 661.
[18] Corbett, Ph.D. Thesis, Birmingham University, 1951.

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Thus, the reduction may be assumed to proceed by the reaction scheme: hydrated form (non-reducible) $\rightleftharpoons$ *aldehydo*-form (reducible), and may be treated by the analysis of Delahay or by that of Los, Simpson, and Wiesner if the presence of anomeric α- and β-forms is disregarded. The limiting current of the *aldehydo*-sugar showed temperature- and pH-dependence typical of kinetically controlled currents. Increase of temperature increased A, B, and $k_s^{\alpha\beta}$ and the plot of log B against the reciprocal of the absolute temperature was linear up to about 25°: the temperature coefficient of A and of B was +14% per degree in the region of 20°. Above 25° the plot had a downward deviation from linearity which may have been caused either by the emergence of diffusion as a rate-controlling factor or by the adoption of a new reduction mechanism having a lower overall activation energy. The activation energy involved in reduction was calculated to be 42 kcal./mole from the gradient of the linear section of the plot of log B against $1/T$.

Values of A, B, and $k_s^{\alpha\beta}$ were determined for 2,4:3,5-di-*O*-ethylidene-*aldehydo*-L-xylose in

TABLE 6. *Polarographic reduction of* 2,4:3,5-*di*-O-*ethylidene*-aldehydo-L-*xylose at various* pH *values at* 25°.

pH	A (microamp. millimole $l.^{-1}$)	B ($sec.^{-1/2}$)	$10^{-5}k_s^{\alpha\beta}$ (cm. $sec.^{-1}$)	Buffer
2·45	0·14	0·017	2·8	KCl–HCl
2·77	0·14	0·017	2·8	K H phthalate–HCl
3·02	0·14	0·017	2·8	
3·61	0·13	0·016	2·7	
4·01	0·10	0·013	2·2	K H phthalate
6·08	0·12	0·015	2·6	Phosphate mixtures
6·62	0·12	0·015	2·5	
7·06	0·17	0·022	3·7	
7·90	0·18	0·023	3·9	Na borate–HCl
9·18	0·83	0·17	28·0	Na borate

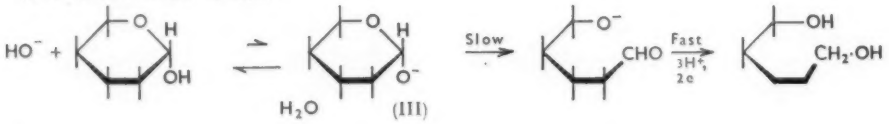
buffer solutions of varying pH, and the polarographic reduction was found to be catalysed by hydrogen and hydroxyl ions (Table 6).

In the pH range 2—6, the velocity of the dehydration reaction is almost independent of pH. The values of the catalytic constants for the dehydration were: $k_{H^+} = 5{\cdot}4 \times 10^2$ l. $mole^{-1}$ $sec.^{-1}$, $k_{OH^-} = 3{\cdot}9 \times 10^7$ l. $mole^{-1}$ $sec.^{-1}$, and $k_{OH^-}/k_{H^+} = 7{\cdot}2 \times 10^4$ at 25°.

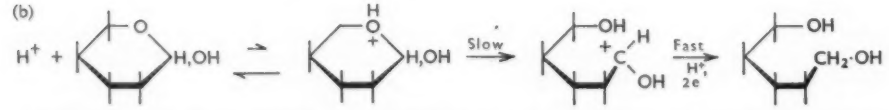
DISCUSSION

Information on the relative stability of the 1-hydrogen atom and 1-hydroxyl group in D-glucose, together with the fact that the product of polarographic reduction of a sugar has been shown to be a polyalcohol, leads to the following proposals for the reduction mechanism.

(a) (Scheme for α-form of sugar)



(b)



Two electrons are required for the reduction of one sugar molecule, as for the reduction of a simple aldehyde to the corresponding alcohol. This assumption is supported by the work of Sugino and Hayashi[19] who showed that the polarographic reduction of D-glucose yielded D-glucitol. The reduction, under alkaline conditions, is considered to proceed by scheme (a) since Fredenhagen and Bonhoeffer[20] demonstrated that the 1-H bond of

[19] Sugino and Hayashi, *J. Chem. Soc., Japan*, 1944, **65**, 458; *Chem. Abs.*, 1947, **41**, 3758*b*.
[20] Fredenhagen and Bonhoeffer, *Z. phys. Chem.*, 1938, **181**, 392.

D-glucose is not broken during alkali-catalysed mutarotations. The intermediate (III) is present in only very small proportion at pH 8 since the pK_a of the 1-hydroxyl group of glucose [21] is of the order of 13. However, the intermediate (III) is removed continuously as reduction proceeds and the reaction shown as scheme (a) is driven to the right-hand side. This mechanism is similar to that proposed by Delahay and Strassner. Both schemes (a) and (b) involve a change from the cyclic to the open-chain form of the sugar and so the rate overall would probably be assisted by any factor which decreases the stability of the ring-form relatively to that of the open-chain or which, in the case of hydroxyl-ion catalysis, facilitates access to the 1-position.

The hexoses generally exhibit lower B values than the pentoses. The B value for ribose appears to be abnormally high but there are other indications, *e.g.*, mutarotation, that ribose shows anomalous behaviour, possibly connected with the higher incidence of furanose forms.

Methylation at the 2-position and, to a smaller extent, at the 3-position, has a marked effect on the B value since 2-*O*-methyl-L-arabinose (0·0057 sec.$^{-1/2}$) and 3-*O*-methyl-D-glucose (0·00063 sec.$^{-1/2}$) both show B values which are considerably lower than those of the parent sugars, L-arabinose (0·028 sec.$^{-1/2}$) and D-glucose (0·0017 sec.$^{-1/2}$). Further, 2,3,4,6-tetra-*O*-methyl-D-glucopyranose appears to be completely non-reducible in concentrations up to 0·1M, the maximum which it was practicable to use with this compound. Similarly, 2,3,4-tri-*O*-methyl-D-ribopyranose shows a lower B value than does D-ribose. Since the rate-determining step is more likely to be that of ring opening in schemes (a) and (b) and since, in acid-catalysis, attack by a hydrogen ion is not usually sterically hindered, such steric effects are more likely to be operative in altering ring stability than in changing the susceptibility to attack by hydrogen or hydroxyl ions, in the first stage of (a) and (b). Moreover, the relatively greater stability of the pyranose ring form, in which these two compounds are constrained, must be of significance.

In contrast, 2-deoxy-D-glucose (0·045 sec.$^{-1/2}$) and, to a smaller extent, 3-deoxy-D-glucose (= 3-deoxy-D-allose; 0·029 sec.$^{-1/2}$) show higher B values than the parent sugar.

2,3,4-Tri-*O*-methyl-L-arabopyranose and 2,3,5-tri-*O*-methyl-D-ribofuranose generated limiting currents which were controlled by the rate of diffusion of the ring form to the mercury drop surface. This indicated that a fast reaction occurred before the electro-reduction stage. When set up in Courtauld-type models [22] these two compounds proved to have very hindered ring structures, so that the ring form is destabilised relatively to the open-chain *aldehydo*-form. Thus, in aqueous solution there are two possibilities: either there is a larger proportion of the *aldehydo*-form of the sugar or there is a high rate of transformation from ring to reducible form. But 2,4:3,5-di-*O*-ethylidene-*aldehydo*-L-xylose, a sugar derivative fixed in the open-chain form (I), has been shown above to generate kinetic currents determined by the dehydration rate of the hydrated form (II). Thus, since 2,3,4-tri-*O*-methyl-L-arabopyranose and 2,3,5-tri-*O*-methyl-D-ribofuranose yield diffusion-controlled currents, they must exist in aqueous solution predominantly as the ring form, but they show a very high rate of transformation to the reducible form. If they existed to an appreciable extent as *aldehydo*-sugars they would be in the hydrated form in aqueous solution and would exhibit kinetic limiting currents.

This work is being continued in an endeavour to obtain further evidence about the steric factors which affect the equilibrium between open-chain and cyclic forms of sugars.

Experimental

Materials.—To obtain clear reproducible polarographic reduction waves it was essential to purify carefully all carbohydrate derivatives. It was necessary to remove alkali-metal impurities which tended to cause coalescence of the buffer and sugar waves. Solid sugars were

[21] Los and Simpson, *Rec. Trav. chim.*, 1954, **73**, 941; 1957, **75**, 267.
[22] Hartley and Robinson, *Trans. Faraday Soc.*, 1952, **48**, 847.

XUM

purified from solvents containing low proportions of water. Syrupy products were distilled under diminished pressure. The following sugars were purified by slow recrystallisation twice from 80% aqueous ethanol and were dried *in vacuo* over phosphoric oxide: α-D-glucose, m. p. 146°, $[\alpha]_D^{20}$ +52·5° (*c* 4 in water); α-D-galactose, m. p. 167—168°, $[\alpha]_D^{20}$ +80·4° (*c* 4 in water); α-D-mannose, m. p. 132°, $[\alpha]_D^{20}$ +14·1° (*c* 4 in water); β-L-arabinose, m. p. 158°, $[\alpha]_D^{20}$ +104° (*c* 4 in water); β-D-lyxose, m. p. 118—119°, $[\alpha]_D^{20}$ −14° (*c* 4 in water); α-D-ribose, m. p. 90°; α-D-xylose, m. p. 146—147°, $[\alpha]_D^{20}$ −18·8° (*c* 4 in water).

Deoxy-sugars were purified to the constants shown: 2-deoxy-D-allose was prepared from methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-alloside [23] by Prins's method.[24] The product was recrystallised from ether to afford the α-form of the sugar, m. p. 126—128°, $[\alpha]_D^{20}$ +150° (*c* 0·6 in $CHCl_3$) (Found: C, 43·8; H, 7·2. Calc. for $C_6H_{12}O_5$: C, 44·0; H, 7·3%); 2-deoxy-β-D-galactose, m. p. 126—128°; 2-deoxy-α-D-glucose (crystallised from methanol–acetone), m. p. 146°; 2-deoxy-β-D-ribose, m. p. 77°; 2-deoxy-β-L-ribose, m. p. 74—76°; 3-deoxy-D-allose, colourless syrup, n_D^{18} 1·4735, $[\alpha]_D^{20}$ +8° (*c* 0·25 in water).

Methylated derivatives: 3-*O*-methyl-D-glucose was prepared by the method of Glen, Myers, and Grant,[25] and was crystallised twice from methanol as white plates, m. p. 167—168°; 3,5,6-tri-*O*-methyl-D-glucofuranose was synthesised by the method of Irvine and Scott [26] as modified by Coles *et al.*[27] and Freudenberg and Vajda.[28] Fractional distillation gave a mobile syrup, b. p. 115—120° (bath-temp.)/0·01 mm., n_D^{15} 1·4549, $[\alpha]_D^{20}$ +39° (*c* 1·1 in methanol) (Found: C, 49·0; H, 8·0; OMe, 41·8. Calc. for $C_9H_{18}O_6$: C, 48·9; H, 8·15; OMe, 42·0%); 2,3,4,6-tetra-*O*-methyl-D-glucose, needles, m. p. 84°, $[\alpha]_D^{20}$ +84·5° (*c* 1 in water); 2-*O*-methyl-L-arabinose, syrup, $[\alpha]_D^{20}$ +61° (*c* 0·18 in water); 2,3,4-tri-*O*-methyl-L-arabinose, prepared by the method of Purdie and Rose [29] except that the methylation was carried out with the Haworth reagent, was a mobile syrup, b. p. 98—99° (bath-temp.)/0·02 mm., n_D^{18} 1·4823, $[\alpha]_D^{20}$ +43° (*c* 0·42 in water) (Found: C, 50·2; H, 8·4; OMe, 48·0. Calc. for $C_8H_{16}O_5$: C, 50·0; H, 8·34; OMe, 48·4%); 2,3,4-tri-*O*-methyl-D-ribose, m. p. 83°; 2,3,5-tri-*O*-methyl-D-ribose,[30] b. p. 75° (bath-temp.)/0·05 mm., n_D^{18} 1·4540, $[\alpha]_D^{20}$ +40° (*c* 1·1 in methanol) (Found: C, 50·1; H, 8·3; OMe, 48·6. Calc. for $C_8H_{16}O_5$: C, 50·0; H, 8·34; OMe, 48·4%).

2,4:3,5-Di-*O*-ethylidene-*aldehydo*-L-xylose was prepared by the method of Bladon and Owen [31] as modified by Corbett.[18] After being recrystallised twice from dry redistilled dioxan it was obtained as needles, m. p. 160—161°, $[\alpha]_D^{20}$ −12·5° (*c* 2 in water).

Buffer solution: the buffer was tetramethylammonium phosphate solution containing phosphoric acid to adjust the pH tc any desired value. Tetramethylammonium iodide (3·015 g.), recrystallised twice from water, in warm distilled water (400 ml.) was mixed with an excess of powdered silver phosphate in a 500 ml. bottle covered with black paper to prevent photodecomposition. (If allowed to proceed unhindered, this decomposition produced much colloidal matter in the buffer and gave large irregularities in the polarographic wave.) The mixture was shaken mechanically overnight and then filtered through a fine Whatman paper to remove silver iodide and the excess of silver phosphate, leaving a clear solution of tetramethylammonium phosphate. 1% Phosphoric acid ("AnalaR") was added to the filtrate to adjust the pH to 8·0 and the solution was diluted to 1 l., giving 0·1M-tetramethylammonium ion. The buffer was stored in a Polythene bottle, and its pH was stable over long periods. The final concentration of tetramethylammonium ion in the solution used in the polarographic cell was 0·002M and this buffer was used throughout unless otherwise stated. Values of pH other than 8 were obtained by variation of the phosphoric acid content.

Methods.—The polarograph was based on the "Voltamoscope" of the Cambridge Instrument Company. The cell was conventional with two side-arms, one for making electrical contact to the pool of mercury at the bottom of the cell, and the other for the passage of hydrogen. The capacity of the cell was 5 ml. Half-wave potentials were measured relative to a saturated calomel electrode which was connected through a saturated potassium chloride

[23] Jeanloz, Prins, and Reichstein, *Experientia*, 1945, **1**, 336; *Helv. Chim. Acta*, 1946, **29**, 371.
[24] Prins, *J. Amer. Chem. Soc.*, 1948, **70**, 3955.
[25] Glen, Myers, and Grant, *J.*, 1951, 2568.
[26] Irvine and Scott, *J.*, 1913, **103**, 564.
[27] Coles, Goodhue, and Hixon, *J. Amer. Chem. Soc.*, 1929, **51**, 519.
[28] Freudenberg and Vajda, *J. Amer. Chem. Soc.*, 1937, **59**, 1955.
[29] Purdie and Rose, *J.*, 1906, **89**, 1204.
[30] Barker, *J.*, 1948, 2035.
[31] Bladon and Owen, *J.*, 1950, 591.

bridge to a side-arm of the polarographic cell. Values of pH were measured by using a bench pH meter in conjunction with a glass electrode. A vigorous stream of pure hydrogen was bubbled through the test solution to remove dissolved oxygen. (Hydrogen was preferred since the smallest traces of oxygen could then be readily removed.)

The experiments were carried out in a water-thermostat at 25° ± 0·05° except where otherwise stated. The galvanometer of the polarograph was calibrated so that limiting currents could be measured directly in microampères. The mercury drop period (τ) was measured with a stop watch, and the mercury flow rate (m) was determined by weighing the mercury dropping from the capillary during a known time interval whilst a voltage corresponding to the " plateau " of the polarographic wave in question was applied between the electrodes. Two capillaries were used: in distilled water at 25° with 480 mm. mercury head and an applied voltage of 2·0 v, the first gave $\tau = 2{\cdot}21$ sec. and $m = 2{\cdot}01$ mg. sec.$^{-1}$; the second gave $\tau = 2{\cdot}87$ sec. and $m = 1{\cdot}429$ mg. sec.$^{-1}$. For each of the sugar solutions studied a residual current–voltage curve was recorded. The difference between this curve and the wave generated by the sugar solution represented the current–voltage curve produced solely by the reduction of the sugar.

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678. *The Reaction of Pyridine with Methyl Propiolate.*

By A. Crabtree, A. W. Johnson, and J. C. Tebby.

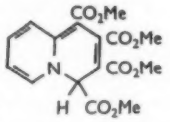
The adducts from pyridine, as well as β- and γ-picoline, and methyl propiolate have been formulated as dihydropyridines (III) containing *N*-β-acrylic ester and β-propiolic ester substituents. Hydrogenolysis of the pyridine adduct gives octahydro-3-oxoindolizine (V), and reaction with piperidine causes cyclisation to methyl (2-methoxycarbonylindolizin-1-yl)-acetate (VII) which has been degraded to octahydro-1-methylindolizine. The Diels rearrangement product of the pyridine–dimethyl acetylenedicarboxylate stable adduct, formed by the action of hot phenol or acetic acid, is formulated as methyl (1,2-dimethoxycarbonylindolizin-3-yl)acetate (X) and has been converted into methyl (2-methoxycarbonylindolizin-3-yl)-acetate (XI; R = Me) and octahydro-3-methylindolizine, both of which differed from the isomers formed in the propiolic ester series. The indolizine formed by reaction of pyridine and dimethyl acetylenedicarboxylate in methanol has been reformulated as methyl (1,2-dimethoxycarbonylindolizin-3-yl)methoxyacetate (XIII) because of its reduction to (X).

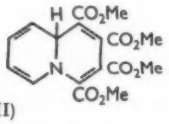
Several authors recently have re-examined the structure of the adducts derived from dimethyl acetylenedicarboxylate with pyridine and related compounds[1,2,3] which were originally described by Diels and his co-workers. There is fairly general agreement in regarding the adducts (*e.g.*, I or a valency tautomer, and II from pyridine) as derivatives of 4*H*- and 9a*H*-quinolizines, and in order to provide further examples of this remarkable reaction we examined the corresponding reactions with methyl propiolate. Pale yellow

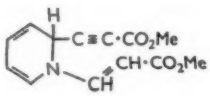
[1] Jackman, Johnson, and Tebby, *J.*, 1960, 1579.
[2] Acheson, Taylor *et al.*, *J.*, 1960, 1691; *Proc. Chem. Soc.*, 1960, 281.
[3] van Tamelen, Aldrich, Bender, and Miller, *Proc. Chem. Soc.*, 1959, 309.

XUM

crystalline adducts were obtained from both pyridine and β-picoline but the absorption spectra (max. at *ca.* 239, 297, and 342 mμ) and the low stability of these products suggested that they possessed a chromophore different from those of the adducts of dimethyl acetylenedicarboxylate.


(I)

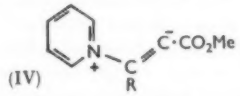

(II)

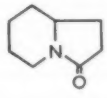

(III)

The pyridine–methyl propiolate adduct decomposed rapidly at 100°, and even at room temperature it decomposed after about six weeks. Analysis indicated that, like the dimethyl acetylenedicarboxylate adducts, each molecule of pyridine had combined with two molecules of the acetylenic ester and, moreover, like the 9a*H*-quinolizines, the adducts were non-basic. Oxidation of the pyridine adduct with hydrogen peroxide in acetic acid gave picolinic acid *N*-oxide, indicating that fission of the pyridine ring had not occurred. The nature of the adducts was revealed by their nuclear magnetic resonance spectra and in consequence structure (III) is advanced for the pyridine–methyl propiolate compound. The spectrum, which was measured and interpreted by Dr. L. M. Jackman, showed bands at 6·28 and 6·24 (methoxy-groups) and doublets at 4·89 and 2·58 (J = 13·4 cycles/sec.; positions expressed as τ values) which were attributed to the two mutually interacting protons of the *cis*-acrylic ester grouping. Examination of the related adduct from γ-picoline showed a band at 8·0 which is attributed to a *C*-methyl group attached to a non-aromatic system. The ultraviolet and visible absorption is consistent [4] with the presence of a 1,2-dihydropyridine ring in the adduct, and the infrared spectrum showed the absence of an >NH grouping and the presence (band at 2235 cm.$^{-1}$) of an acetylenic bond.

In considering the mechanisms of the formation of the pyridine–acetylenic ester adducts (I), (II), and (III), the key intermediates are probably the ylids (IV; R = H or CO_2Me) formed by nucleophilic addition of an equimolecular amount of the pyridine to the acetylenic ester. The ylid (IV; R = CO_2Me) from dimethyl acetylenedicarboxylate can then react with a second equivalent of the acetylenic ester to give a second ylid, which can cyclise to the quinolizine (II), as has been suggested previously.[1] In the case of the methyl propiolate adducts, the ylid (IV; R = H) reacts wth a proton formed by ionisation of another molecule of the acetylenic ester and the remaining acetylenic carbanion adds to the pyridinium ring to form the adduct (III).

In support of the formulation (III) for the propiolic ester adduct, hydrogenation under pressure over Raney nickel at 120° gave an oil which showed a strong infrared band at


(IV)

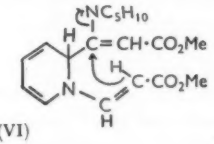

(V)

1690 cm.$^{-1}$ indicative of the carbonyl group of an amide, and on this basis, coupled with the analytical figures, the hydrogenation product is formulated as octahydro-3-oxoindolizine (V). This amide [5] was shown to possess an infrared spectrum identical with that of the degradation product. Hydrogenolysis of the adduct (III) presumably involves loss of the acrylic ester side-chain and evidence for the presence of an aliphatic ester (methyl propionate?) in the volatile products from the reaction was obtained from the infrared spectrum (band at 1745 cm.$^{-1}$). Octahydro-3-oxoindolizine was further reduced

[4] Karrer *et al.*, *Helv. Chim. Acta*, 1957, **40**, 751; 1958, **41**, 2066; "Festschrift A. Stoll," Basel, 1957, p. 294.
[5] Tullock and McElvain, *J. Amer. Chem. Soc.*, 1939, **61**, 961.

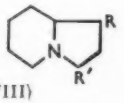
by lithium aluminium hydride, to octahydroindolizine itself which was identified as the picrate.[6]

In an attempt to bring about interaction of the two side-chains of the adduct (III), by first hydrating the propiolic ester side-chain, piperidine was caused to react with the activated triple bond, a colourless crystalline compound, $C_{13}H_{13}NO_4$, being obtained. The hydrogen content of this indicated that a piperidyl group was not present and the ultra-



(VI)

(VII)



(VIII)

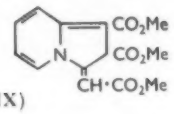
violet absorption spectrum revealed that the product was an indolizine. Taking into account the most probable reaction sequence suggested in (VI), we represent the product as methyl (2-methoxycarbonylindolizin-1-yl)acetate (VII).

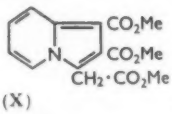
The dicarboxylic acid and anhydride corresponding to (VII) were also prepared and the acid decarboxylated to 1-methylindolizine which was hydrogenated to the octahydroindolizine (VIII; R = Me, R′ = H) and converted to the picrate.[7] This base should exist as two racemates depending on the relative configurations of the methyl substituent and the bridgehead hydrogen atom, but in this case a separation could not be achieved with the small quantity available. Consequently the melting point (184—189°; lit.,[7] 191°) of the picrate was not sharp, and the identity or otherwise of this base with the isomeric 3-methylindolizidines where the two forms have been separated [8] (picrates, m. p. 195—197° and 216°) remained in doubt until these compounds were prepared.

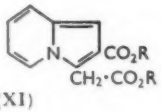
Condensation of α-picoline and propionic anhydride [9] gave, in low yield, 3-methylindolizine which was hydrogenated to octahydro-3-methylindolizine (VIII; R = H, R′ = Me), from which, however, only the lower-melting (190—193°) picrate could be isolated. Fortunately another sequence of reactions was discovered which left no doubt that the hydrogenation product from the rearrangement of the pyridine–propiolic ester adduct differed from octahydro-3-methylindolizine. Rearrangement of the stable adduct (I) from pyridine and dimethyl acetylenedicarboxylate by treatment with hot acetic acid or phenol is known [10,11] to yield a tricarboxylic ester which from its ultraviolet absorption curve is undoubtedly a derivative of indolizine. Since this manuscript was written, Acheson and Taylor [12] have reached a similar conclusion. Originally,[10] Diels and his co-workers thought that this ester was a derivative of quinolizine, but later, structure (IX) was preferred. By use of the sequence developed by Diels originally for the preparation of quinolizine itself (later shown to be an indolizine, however), the tricarboxylic ester, for which the modified structure (X) is suggested, was hydrolysed with aqueous potassium hydroxide, a dicarboxylic acid being obtained. Although Acheson and Taylor [12] suggest that this acid may be 3-methylindolizine-1,2-dicarboxylic acid rather than 2-carboxyindolizin-3-ylacetic acid (XI; R = H) on the grounds that the corresponding tetrahydroderivative gives approximately one-sixth of the theoretical quantity of acetic acid in the Kuhn–Roth determination, we are adopting the latter structure on the grounds of the nuclear magnetic resonance spectrum kindly determined and interpreted for us by Dr. R. J. Abraham of the National Physical Laboratory, Teddington. Examination of the spectrum showed peaks associated with the methylene group as well as the single isolated aromatic

[6] Clemo and Ramage, *J.*, 1932, 2969.
[7] Clemo and Metcalf, *J.*, 1937, 1518.
[8] Leonard and Pines, *J. Amer. Chem. Soc.*, 1950, **72**, 4931.
[9] Ochiai and Tsuda, *Ber.*, 1934, **67**, 1011.
[10] Diels, Alder, Friedrichsen, Klare, *et al.*, *Annalen*, 1932, **498**, 16; 1933, **505**, 103.
[11] Diels and Schrumm, *Annalen*, 1937, **530**, 68.
[12] Acheson and Taylor, *J.*, 1960, 4600.

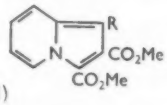
proton, but peaks associated with an aromatic *C*-methyl group were absent. The corresponding dimethyl ester (XI; R = Me) was markedly different from the ester (VII) derived from the pyridine–propiolic ester adduct and emphasises the isomeric nature of the two series. Decarboxylation of the acid (XI; R = H) gave 3-methylindolizine,

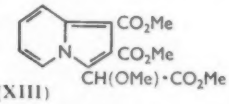

(IX)


(X)


(XI)

hydrogenated to the octahydro-compound (VIII; R = H, R′ = Me) which gave two distinct picrates corresponding to the two racemates.[8] Diels and Schrumm [11] reported only the lower-melting picrate; the higher-melting picrate, which Diels also obtained [10,11]


(XII)


(XIII)

but associated with octahydroindolizine itself, was possibly the derivative of the other racemate of octahydro-3-methylindolizine.

The formation of the tricarboxylic ester (X) emphasises the instability of the 4*H*-quinolizine ring and provides another example of the strong tendency to revert to the aromatic indolizine ring system. Recent interpretations [3,13] of the nuclear magnetic resonance spectra of 4*H*-quinolizines have in fact suggested that these compounds might be more correctly regarded as 2-pyridylbuta-1,3-dienes.

Another series of adducts from pyridines and acetylenic esters requires consideration in view of the above observations. Diels and Meyer [14] showed that pyridine and dimethyl acetylenedicarboxylate in cold methanol afforded a mixture of two indolizine tricarboxylic esters which were formulated as [XII; R = CO_2Me and $CH(OMe)\cdot CO_2Me$]. We have now shown that the adduct of supposed structure [XII; R = $CH(OMe)\cdot CO_2Me$] can be reduced with phosphorus and iodine in acetic acid solution to the diester of an indolizinetricarboxylic acid, which, when esterified with diazomethane, gives the tricarboxylic ester (X). Further, treatment of the ester (X) with phosphorus and iodine as before causes hydrolysis of one ester grouping and forms the same indolizinetricarboxylic acid diester. Consequently, Diels's formulation [XII; R = $CH(OMe)\cdot CO_2Me$] of his adduct must be modified to (XIII). The precise intermediates in the formation of (XIII) have not yet been defined as it has not proved possible to rearrange ester (I) or (II) to (XIII) with methanol alone, with methanolic sodium methoxide, or with acidified methanol.

Adducts corresponding to (X), (XI), and (XIII) have been prepared from β-picoline and, as in the case of the corresponding quinolizine derivatives,[1] differences in chemical behaviour result from the position of the methyl group which can be a 6- or an 8-substituent. In the latter case, steric hindrance results from the proximity of the methyl and the 1-methoxycarbonyl group and this is revealed for example in the hydrolysis of the analogues of (X). With the 8-methyl compound, decarboxylation of the 1-carboxyl group is an easy reaction accompanying hydrolysis, and the product is a dicarboxylic ester, whereas with the 6-methyl isomer, the product is the diester of a tricarboxylic acid.

Experimental

Ultraviolet absorption spectra refer to ethanolic solutions and infrared spectra to potassium bromide discs except where otherwise stated.

[13] Elvidge and Jackman, *J.*, 1961, 859.
[14] Diels and Meyer, *Annalen*, 1934, **513**, 129; see also Burrows and Holland, *J.*, 1947, 672.

Reaction of Pyridine and Methyl Propiolate.—Pure dry pyridine (0·5 g.) in dry ether (2 c.c.) was added dropwise to a solution of methyl propiolate [15] (1 g.) in ether (1 c.c.) at room temperature. The solution slowly darkened and was dark red after 1 hr. Next morning the crystalline adduct (III) [*methyl* cis-β-(1,2-*dihydro*-2-*methoxycarbonylethynyl*-1-*pyridyl*)*acrylate*] (0·8 g.) was separated and washed with a little dry ether. On crystallisation from cyclohexane, it was obtained as biscuit-coloured plates, m. p. 98° (decomp.), which were easily decomposed by heat (Found: C, 62·9; H, 5·5; N, 5·75. $C_{13}H_{13}NO_4$ requires C, 63·15; H, 5·3; N, 5·65%), $\lambda_{max.}$ 239, 297, and 342 mμ (log ε 3·90, 3·95, and 4·08 respectively), $\nu_{max.}$ 714, 909, 924, 972, 989, 1018, 1036, 1056, 1075, 1135, 1170, 1197, 1227, 1253, 1286, 1319, 1340, 1357, 1384, 1388, 1437, 1460, 1586, 1631, 1712, 1726, 2235, 2844, 2905, 2950, 2998, and 3060 cm.$^{-1}$.

Reaction of β-Picoline and Methyl Propiolate.—The *adduct* was obtained by a similar method except that the reaction mixture was kept for 2 days and the product was crystallised from methanol at −50°. It formed colourless needles which were unstable to heat; the m. p. varied considerably, 82° to 94°, with the rate of heating (Found: C, 64·1; H, 5·95; N, 5·2. $C_{14}H_{15}NO_4$ requires C, 64·35; H, 5·8; N, 5·35%). Light absorption: max. were at 238 and 339 mμ (log ε 4·05 and 4·04). This adduct was markedly less stable than those from either pyridine or γ-picoline.

Reaction of γ-Picoline and Methyl Propiolate.—Methyl propiolate (4 g.) in dry ether (10 c.c.) was added dropwise with stirring to γ-picoline (2 g.) in dry ether (10 c.c.) and kept at room temperature for 1 hr. The precipitate (2·5 g.) was separated, washed with dry ether (20 c.c.), and crystallised from cyclohexane, to give *methyl* cis-β-(1,2-*dihydro*-2-*methoxycarbonylethynyl*-4-*methyl*-1-*pyridyl*)*acrylate* as pale orange plates, m. p. 115—116° (Found: C, 64·6; H, 6·05; N, 5·15%), $\lambda_{max.}$ 244 and 337 mμ (log ε 3·94 and 4·12), $\nu_{max.}$ 745, 754, 772, 797, 816, 846, 922, 945, 977 984, 1000, 1029, 1038, 1052, 1082, 1153, 1170, 1188, 1202, 1238, 1275, 1314, 1346, 1380, 1434, 1444, 1461, 1486, 1582, 1597, 1633, 1674, 1715, 1722, 2225, 2857, 2920, 2960, 2977, 3018, 3050, and 3398 cm.$^{-1}$. The adduct was kept without decomposition for several months.

Oxidation of the Pyridine–Methyl Propiolate Adduct.—The adduct (2 g.) was dissolved in glacial acetic acid (40 c.c.) and 100-vol. hydrogen peroxide (20 c.c.) and the mixture heated on the steam-bath for 2 hr. The excess of solvent was then removed *in vacuo*, and the oily residue treated with a similar volume of glacial acetic acid and hydrogen peroxide and heated on the steam-bath overnight. The solvent was again removed and the residue extracted with boiling cyclohexane (5 × 20 c.c.). When the mixed extracts were cooled picolinic acid *N*-oxide was obtained as white needles, m. p. 166° (from methanol) not depressed on admixture with an authentic specimen [16] (Found: C, 51·6; H, 3·6; N, 10·0. Calc. for $C_6H_5NO_3$: C, 51·8; H, 3·6; N, 10·05%), $\lambda_{max.}$ 224, 264, and 311 mμ (log ε 4·28, 3·85, and 3·11 respectively).

Octahydro-3-*oxoindolizine* (V).—The pyridine–methyl propiolate adduct (3 g.) in methanol (300 c.c.) was shaken at room temperature with Raney nickel (0·2 g.) in an atmosphere of hydrogen (60 atm.) for 3 hr. The temperature was then raised to 120° for a further 10 hr., then the catalyst and solvent were removed and the residue was distilled at 70—80° (bath-temp.)/0·5 mm. to give octahydro-3-oxoindolizine as a colourless, slightly fluorescent oil (1 g.) (Found: N, 9·85. Calc. for $C_8H_{13}NO$: N, 10·05%). A hydrochloride [17] could be formed but was very deliquescent and sublimed at 140°/0·1 mm. Reduction of this amide with lithium aluminium hydride [18] gave octahydroindolizine (0·2 g.), b. p. (bath-temp.) 60—70°/15 mm., the infrared spectrum of which was identical with an authentic specimen prepared by reduction of authentic amide.[5,6] The picrate had m. p. 226° (lit.,[6] 226°).

In another experiment the pyridine–methyl propiolate adduct (2 g.) was hydrogenated in purified 2-methoxyethanol (40 c.c.) as in the previous experiment. After cooling, the hydrogen was blown off through a cold (−60°) trap and the small amount of liquid so collected in the trap was shown to possess a weak infrared band at 1745 cm.$^{-1}$ (saturated ester). The catalyst was removed from the main product and the first fraction (3 c.c.) from the solvent distillation was also shown to give this ester band.

Reaction of the Pyridine–Methyl Propiolate Adduct with Piperidine.—The adduct (1·5 g.) in dry benzene (20 c.c.) was added dropwise with shaking to piperidine (2 c.c.) in dry benzene (10 c.c.) and the mixture heated under reflux for 1 hr., becoming dark red. The solvents were

[15] Wolf, *Chem. Ber.*, 1953, **86**, 735; Bielecki and Henri, *ibid.*, 1913, **46**, 2605.
[16] Emmert and Groll, *Chem. Ber.*, 1953, **86**, 205.
[17] Loffler and Kain, *Chem. Ber.*, 1909, **42**, 100.
[18] Galinovsky, Vogl, and Weisser, *Monatsh.*, 1952, **83**, 114.

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removed and the residue was distilled, to give a yellow oil, b. p. (bath-temp.) 150—200°/0·1 mm., which slowly crystallised. Recrystallisation from cyclohexane gave colourless needles of *methyl* (*2-methoxycarbonylindolizin-1-yl*)*acetate* (VII), m. p. 88—89° (Found: C, 63·3; H, 5·3; N, 5·6. $C_{13}H_{13}NO_4$ requires C, 63·3; H, 5·3; N, 5·7%), $\lambda_{max.}$ 236, 295, 306, 352, 367, and 385 mμ (log ε 4·61, 3·34, 3·38, 3·41, 3·42, and 3·19 respectively), $\nu_{max.}$ 744, 755, 788, 806, 841, 896, 903, 937, 958, 989, 999, 1016, 1097, 1125, 1166, 1183, 1202, 1217, 1256, 1268, 1316, 1341, 1364, 1409, 1426, 1438, 1449, 1460, 1498, 1538, 1635, 1662, 1705, 1728, 1737, 2367, 2925, 2950, 2978, 3047, 3106, and 3140 cm.$^{-1}$. Alkaline hydrolysis gave the corresponding *acid*, which formed almost colourless needles, decomp. 210°, from 80% aqueous ethanol (Found: C, 60·0; H, 4·2; N, 6·55. $C_{11}H_9NO_4$ requires C, 60·3; H, 4·15; N, 6·4%), $\lambda_{max.}$ 236, 295, 306, 353, and 368 mμ (log ε 4·60, 3·33, 3·38, 3·42, and 3·42) (inflection at 390 mμ; log ε 3·15), $\nu_{max.}$ 745, 944, 960, 1105, 1135, 1165, 1175, 1192, 1212, 1229, 1258, 1280, 1300, 1318, 1356, 1403, 1417, 1448, 1469, 1498, 1543, 1632, 1650, 1681, 1699, 2600, 2658, 2940, 3125, and 3585 cm.$^{-1}$.

The acid (0·7 g.) was heated with acetic anhydride (1·5 c.c.) for 3 hr. at 140—150°; much charring occurred. After removal of the excess of solvent *in vacuo*, the residue was sublimed at 140°/0·05 mm., to yield the *anhydride* as a yellow solid (40 mg.), decomp. 200° (Found: C, 65·7; H, 3·75; N, 6·7. $C_{11}H_7NO_3$ requires C, 65·7; H, 3·5; N, 6·95%), $\lambda_{max.}$ (in *NN*-dimethylformamide) 258, 305, 357, 374, and 436 mμ (log ε 4·01, 3·52, 3·48, 3·46, and 3·06 respectively), $\nu_{max.}$ 1759s and 1780s cm.$^{-1}$ associated with the six-membered anhydride grouping.

Octahydro-1-methylindolizine (VIII; R = Me, R′ = H).—The foregoing dicarboxylic acid (6 g.) was intimately mixed with finely powdered calcium oxide (40 g.); the mixture, in small portions (3—4 g.), was heated strongly and the distillate collected. The combined distillates (3 c.c.) were mixed with 10% sodium hydroxide solution (5 c.c.) and steam-distilled. The rather unstable oil obtained in the distillate was isolated by extraction with ether and hydrogenated in methanol over Raney nickel at 180°/200 atm. After removal of the solvent, the residual oil (1 g.) was converted into the picrate which formed yellow plates, m. p. 184—189° (lit.,[7] 191°), from methanol.

Octahydro-3-methylindolizine (VIII; R = H, R′ = Me).—(i) 3-Methylindolizine was prepared by condensation of α-picoline and propionic anhydride by Ochiai and Tsuda's method.[9] The product was hydrogenated in methanol at 180°/200 atm. over Raney nickel. After removal of the catalyst and solvent, the resulting base was converted into the picrate which formed yellow needles, m. p. 190—193°. Attempted separation of the two forms of the base by chromatography on alumina (cf. ref. 8) yielded only one major fraction which gave a picrate, m. p. 194°, identical with the product described below. The higher-melting form was not obtained.

(ii) (2-Carboxyindolizin-3-yl)acetic acid (4·3 g.) (XI; R = H) was intimately mixed with powdered calcium oxide and distilled in six portions from a bulb tube. The combined distillates were extracted with ether, the solvent was then removed, and the residue distilled in steam. The distillate was extracted with ether and from the dried extract 3-methylindolizine was obtained as a pale yellow oil (1·5 g.), the infrared spectrum of which (in CCl_4) showed max. at 682, 702, 884, 958, 1000, 1020, 1070, 1113, 1145, 1235, 1267, 1295, 1310, 1350, 1370, 1390, 1440, 1490, 1615, 1670, 1715, 1745, 1810, 1880, 2850, 2910, 2990, and 3070 cm.$^{-1}$. The *picrate* formed blue needles, m. p. 95—96°, from ethanol (Found: C, 50·0; H, 3·5. $C_9H_9N,C_6H_3N_3O_7$ requires C, 50·0; H, 3·3%), $\lambda_{max.}$ 234, 282, 295, and 354 mμ (log ε 4·65, 3·91, 3·96, and 3·09 respectively).

The above base (1·5 g.) in methanol (100 c.c.) was hydrogenated overnight over Raney nickel (0·75 g.) at 180°/180 atm. After removal of the catalyst, the solvent was removed (fractionating column; product very volatile), leaving octahydro-3-methylindolizine as a pale yellow oil (0·15 g.), $\nu_{max.}$ 904, 1054, 1112, 1140, 1185, 1245, 1293, 1310, 1360, 1430, 1440, 2770, 2840, and 2925 cm.$^{-1}$. The picrate (0·25 g.), when crystallised from methanol, gave a first fraction (0·1 g.), m. p. 208—209°, as bright yellow needles and a second fraction (0·07 g.), m. p. 192—193°, as dull yellow prisms from the mother-liquors. The latter picrate was identical with the product obtained by method (i).

Methyl (*1,2-Dimethoxycarbonylindolizin-3-yl*)*acetate* (X).—Prepared by heating tetramethyl-4*H*-quinolizine-1,2,3,4-tetracarboxylate with phenol [10] and crystallised from 50% methanol, this formed colourless needles, m. p. 70° (lit., 75°,[10] 68° [12]) (Found: C, 59·0; H, 5·2; N, 4·8; OMe, 31·2. Calc. for $C_{15}H_{15}NO_6$: C, 59·0; H, 4·9; N, 4·6; 3OMe, 30·5%), $\lambda_{max.}$ 219, 245, 293, 305, and 346 mμ (log ε 4·30, 4·40, 3·74, 3·89, and 3·86 respectively), $\lambda_{infl.}$ 335 mμ (log ε, 3·84).

$\nu_{max.}$ 700, 728, 742, 747, 771, 787, 837, 893, 937, 945, 975, 993, 1003, 1022, 1044, 1105, 1136, 1163, 1187, 1211, 1250, 1278, 1322, 1346, 1363, 1397, 1402, 1418, 1438, 1444, 1453, 1513, 1532, 1563, 1639, 1690, 1721, 1727, 2955, 3002, 3098, 3444, and 3557 cm.$^{-1}$.

Methyl (1,2-*Dimethoxycarbonyl*-8-*methylindolizin*-3-*yl*)*acetate*.—Tetramethyl 9-methyl-4*H*-quinolizine-1,2,3,4-tetracarboxylate [1] (3·2 g.), m. p. 208°, one of the stable adducts from β-picoline and dimethyl acetylenedicarboxylate, was heated with glacial acetic acid (32 c.c.) for 20 min. The solvent was removed under reduced pressure, methanol (20 c.c.) was added, and the mixture cooled. The solid was separated, washed with methanol, and dried; it formed colourless cubes (2·55 g.), m. p. 105—106° [Found: C, 60·3; H, 5·6; N, 4·5%; *M* (Rast), 301. $C_{16}H_{17}NO_6$ requires C, 60·2; H, 5·3; N, 4·4%; *M*, 319], $\lambda_{max.}$ 241, 292, 303, 341, and 349 mμ (log ε 4·53, 3·60, 3·70, 3·66, and 3·65), $\nu_{max.}$ 1711 and 1737 (C=O) cm.$^{-1}$.

By a similar method, tetramethyl 7-methyl-4*H*-quinolizine-1,2,3,4-tetracarboxylate [1] (1·5 g.), m. p. 224°, was rearranged with acetic acid and the product crystallised from 50% methanol to yield colourless needles of *methyl* (1,2-*dimethoxycarbonyl*-6-*methylindolizin*-3-*yl*)*acetate*, m. p. 110° (Found: C, 60·2; H, 5·1; N, 4·6; OMe, 28·8%), $\lambda_{max.}$ 220, 249, 296, 308, and 347 mμ (log ε 4·37, 4·48, 3·70, 3·83, and 3·93 respectively), $\lambda_{infl.}$ 335 mμ (log ε 3·90), $\nu_{max.}$ 1698 and 1728 (C=O) cm.$^{-1}$.

(2-*Carboxyindolizin*-3-*yl*)*acetic Acid* (XI; R = H).—Prepared by alkaline hydrolysis [10] of methyl (1,2-dimethoxycarbonylindolizin-3-yl)acetate, the acid formed colourless needles, m. p. 220° (decomp.) (lit.,[10] m. p. 229°), from 60% acetic acid (Found: C, 60·4; H, 4·5; N, 6·45. Calc. for $C_{11}H_9NO_4$: C, 60·3; H, 4·1; N, 6·4%), $\lambda_{max.}$ 235, 290, 301, 352, 364, and 385 mμ (log ε 4·64, 3·36, 3·40, 3·42, 3·42, and 3·19), $\nu_{max.}$ 725, 742, 767, 817, 851, 923, 980, 1015, 1100, 1139, 1174, 1215, 1247, 1283, 1325, 1346, 1370, 1397, 1428, 1449, 1526, 1556, 1674, 1707, 2348, 2370, 2607, 2640, 2675, 2757, 2860, 2937, 3030, 3076, 3130, and 3425 cm.$^{-1}$.

The dimethyl ester obtained therefrom by methanolic hydrogen chloride formed colourless prisms (from cyclohexane), m. p. 120—121° (Found: C, 63·3; H, 5·2; N, 5·6; OMe, 24·3. $C_{13}H_{13}NO_4$ requires C, 63·2; H, 5·3; N, 5·7; 2OMe, 25·0%), $\lambda_{max.}$ 235, 291, 302, 350, 365, and 384 mμ (log ε 4·66, 3·38, 3·44, 3·38, 3·42, and 3·19 respectively), $\nu_{max.}$ 1710 and 1732 (C=O) cm.$^{-1}$.

Methyl (1,2-*Dimethoxycarbonylindolizin*-3-*yl*)*methoxyacetate* (XIII).—Prepared [11] by reaction of pyridine (6 c.c.) and dimethyl acetylenedicarboxylate (11 c.c.) in methanol (30 c.c.), originally in an acetone–carbon dioxide bath and then allowed to warm slowly to 0°, this ester was kept at 0° for 2 days, after which the crystalline product (2·65 g.), m. p. 119—125°, was separated and crystallised repeatedly from methanol; it then had m. p. 139—140° (lit.,[13] 142—143°) (Found: C, 57·3; H, 5·25; N, 4·35; OMe, 37·6. Calc. for $C_{16}H_{17}NO_7$: C, 57·3; H, 5·1; N, 4·2; 4OMe, 37·0%), $\lambda_{max.}$ 218, 244, 269, 305, and 337 mμ (log ε 4·33, 4·48, 3·81, 3·97, and 3·92), $\nu_{max.}$ 693, 732, 747, 767, 774, 788, 826, 836, 899, 960, 990, 1022, 1042, 1097, 1116, 1188, 1213, 1223, 1247, 1282, 1301, 1336, 1362, 1400, 1427, 1438, 1465, 1517, 1567, 1700, 1719, 1754, 2600, 2840, 2955, 3008, 3290, and 3565 cm.$^{-1}$.

Methyl (1,2-*Dimethoxycarbonyl*-6-*methylindolizin*-3-*yl*)*methoxyacetate*.—Prepared by a similar method from β-picoline (9·6 g.) and dimethyl acetylenedicarboxylate (18 c.c.), the *adduct* formed colourless rods (1·1 g.), m. p. 159—160°, from methanol (Found: C, 58·6; H, 5·2; N, 4·1. $C_{17}H_{19}NO_7$ requires C, 58·5; H, 5·5; N, 4·0%), $\lambda_{max.}$ 218, 248, 308, and 339 mμ (log ε 4·34, 4·52, 3·88, and 3·95 respectively), $\nu_{max.}$ 1701, 1718, and 1747 (C=O) cm.$^{-1}$.

This adduct (0·65 g.) with 100-vol. hydrogen peroxide (6 c.c.) in glacial acetic acid (3 c.c.) at 100° for 1 hr., the solvent was removed *in vacuo*, and crystallisation of the residue from methanol (5 c.c.) gave 5-methylpicolinic acid *N*-oxide as colourless needles (0·07 g.), m. p. 160—161° alone and mixed with a specimen, m. p. 161—162°, prepared by a similar oxidation of tetramethyl 7-methyl-4*H*-quinolizine-1,2,3,4-tetracarboxylate.[1] The oxide had $\lambda_{max.}$ 228 and 267 mμ (log ε 4·4 and 3·9) (Acheson and Taylor [2] gave 253 mμ, 3·85, by an error of transcription).

Methyl (1-*Carboxy*-2-*methoxycarbonylindolizin*-3-*yl*)*acetate*.—(i) Methyl (1,2-dimethoxycarbonylindolizin-3-yl)methoxyacetate (see above; m. p. 139—140°; 1·5 g.) was added to iodine (0·25 g.) and red phosphorus (0·75 g.) in glacial acetic acid (12·5 c.c.) and heated under reflux for 3 hr. The solid was separated from the hot solution, and the filtrate added to a solution of sodium dithionite (1·25 g.) in water (50 c.c.) and kept at 0° overnight. The product was separated, washed with hot methanol (5 c.c.), and crystallised from methanol as colourless needles (0·15 g.), m. p. 199—200°, identical with the product of the following experiment.

(ii) Methyl (1,2-dimethoxycarbonylindolizin-3-yl)acetate (see above; m. p. 65—66°; 1·5 g.) was treated as described in the previous experiment. The monocarboxylic *acid* again had m. p.

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199—200° [Found: C, 57·3; H, 4·5; N, 4·5; OMe, 19·0%; equiv. (titration), 281. $C_{14}H_{13}NO_6$ requires C, 57·7; H, 4·5; N, 4·8; 2OMe, 21·3%; equiv., 291], $\lambda_{max.}$ 219, 250, 309, 337, 352, and 370 mμ, (log ε 4·28, 4·43, 3·83, 3·98, 4·08, and 3·92 respectively), $\nu_{max.}$ 725, 757, 777, 840, 877, 904, 950, 984, 992, 1031, 1040, 1113, 1157, 1178, 1218, 1244, 1254, 1294, 1357, 1386, 1405, 1438, 1456, 1483, 1500, 1523, 1552, 1604, 1637, 1712, 1728, 2315, 2450, 2501, 2580, 2850, 2958, 3001, 3030, 3092, 3123, 3143, and 3444 cm.$^{-1}$.

Methylation with diazomethane gave methyl (1,2-dimethoxycarbonylindolizin-3-yl)acetate, m. p. 64—65° not depressed when mixed with an authentic specimen (above). The ultraviolet and infrared spectra were identical with those of the previous sample.

Methyl (1-Carboxy-2-methoxycarbonyl-6-methylindolizin-3-yl)acetate.—Treatment of methyl (1,2-dimethoxycarbonyl-6-methylindolizin-3-yl)acetate, m. p. 110° (above), with iodine and phosphorus in acetic acid as in the preceding experiments gave the corresponding *1-carboxylic acid*, m. p. 240—241°, as colourless needles (Found: N, 4·45; OMe, 19·4. $C_{15}H_{15}NO_6$ requires N, 4·6; 2OMe, 20·3%), $\lambda_{max.}$ 221, 253, 299, 312, 339, 353, and 371 mμ (log ε 4·33, 4·45, 3·61, 3·71, 3·98, 4·10, and 3·53 respectively), $\nu_{max.}$ 1713 and 1737 (C=O) cm.$^{-1}$.

A similar experiment with methyl (1,2-dimethoxycarbonyl-8-methylindolizin-3-yl)acetate caused decarboxylation as well as hydrolysis of the 1-methoxycarbonyl group and formed *methyl (2-methoxycarbonyl-8-methylindolizin-3-yl)acetate*, m. p. 130—132°, as colourless needles (methanol) (Found: C, 64·3; H, 5·7; N, 5·7; OMe, 23·0. $C_{14}H_{15}NO_4$ requires C, 64·4; H, 5·7; N, 5·4; 2OMe, 23·8%), $\lambda_{max.}$ 236, 290, 301, 344, 360, and 378 mμ (log ε 4·72, 3·53, 3·59, 3·52, 3·55, and 3·37 respectively).

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THE UNIVERSITY, NOTTINGHAM. [*Received, February 16th*, 1961.]

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679. *Steroids Derived from Hecogenin. Part II.*[1] *Some Ring C-Seco-derivatives.*

By PETER BLADON and W. MCMEEKIN.

The Baeyer–Villiger oxidation of hecogenin acetate gives, besides the known hecololactone acetate, some 5% of the isomeric isohecololactone acetate. Derivatives of this lactone and of the corresponding acid are described.

The reaction between methyl hecolate and an excess of phenylmagnesium bromide or phenyl-lithium proceeded only to the stage of the phenyl ketone (VI). This ketone was readily cyclised to the enol ether (VII).

The lactam produced by Beckmann rearrangement of hecogenin acetate oxime was converted into derivatives of hecolic acid, this being a proof of the structure (X) for the lactam.

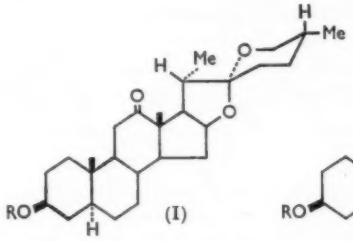
IN 1954 Rothman, Wall, and Eddy[2] reported the formation of a lactone by the Baeyer–Villiger oxidation of hecogenin acetate (I; R = Ac). This lactone, to which they gave the name hecololactone acetate, was hydrolysed to the corresponding acid, hecolic acid. The transformations which the lactone and the acid underwent led these workers to ascribe[3] to them the undoubtedly correct structures (II; R = Ac) and (III; R = R′ = H).

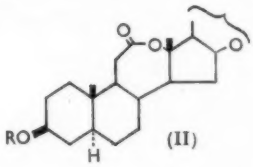
Methyl hecolate (III; R = H, R′ = Me) seemed a suitable starting material for a Barbier–Wieland reaction. We prepared hecolic acid by the second of two published

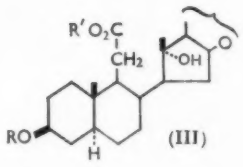
[1] Part I, Bladon and McMeekin, *J.*, 1960, 2191.
[2] Rothman, Wall, and Eddy, *J. Amer. Chem. Soc.*, 1954, **76**, 527.
[3] Rothman and Wall, *J. Amer. Chem. Soc.*, 1955, **77**, 2228, 2229.

XUM

methods,[2] involving oxidation of hecogenin with peracetic acid in a two-phase system in the presence of sulphuric acid. The resulting crude lactone mixture was hydrolysed directly to a mixture of acids that gave on crystallisation 82% of hecolic acid and 5% of a

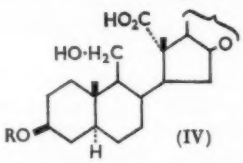

(I)

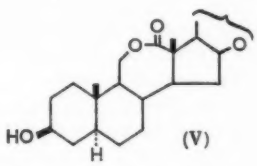

(II)


(III)

second, isomeric acid which we call isohecolic acid (sparing solubility of the former in chloroform made this separation feasible). Isohecolic acid formed a methyl ester, whose diacetate no longer had infrared absorption characteristic of a hydroxyl group These facts show that isohecolic acid has structure (IV; R = R′ = H), formed by the alternative fission of ring C.

Isohecolic acid readily lactonised *in vacuo* above its melting point, giving a lactone (V), characterised as its acetate and benzoate.


(IV)


(V)

The melting points in the iso series are in general higher than in the isomeric series, and the optical rotations also differ. In the infrared spectra carbonyl absorption of the iso-compounds tends to occur at lower frequency than in the normal series.

Two fractions of neutral material were encountered in the preparation of the acids. The first was a mixture of unchanged hecogenin, tigogenin, and 9(11)-dehydrohecogenin, the last two being known impurities in the hecogenin used (cf. ref. 2). The second was a mixture of unhydrolysed (or perhaps recyclised) lactones. Hydrolysis of this gave hecolic and isohecolic acid, together with a small quantity of a third acid (acid C), which were separated by crystallisation. Acid C is not a mixture of hecolic and isohecolic acid since its optical rotation is more negative than that of either. So far the small amount available has precluded further work on it. It is possibly the 13β-hydroxy-isomer of hecolic acid.

Treatment of methyl hecolate with an excess of phenylmagnesium bromide under the usual Barbier–Wieland conditions [4] or with phenyl-lithium resulted in the uptake of only one mole of reagent. The product, in neither case crystalline, had an ultraviolet spectrum ($\lambda_{max.}$ 242 mμ) similar to that of propiophenone [5] ($\lambda_{max.}$ 242 mμ), consistently with its formulation as the phenyl ketone (VI). On acetylation followed by brief treatment with boiling acetic acid, this compound was dehydrated to a crystalline product formulated as (VII; R = Ac). The ultraviolet spectrum ($\lambda_{max.}$ 205, 218, 263 mμ) was fairly consistent with this formulation, its difference from that of the analogous β-methylstyrene [5] ($\lambda_{max.}$ 251 mμ) being attributable to the influence of the ethereal oxygen atom. Good yields of this compound were obtained only under anhydrous conditions, since, when it was heated

[4] Riegel, Moffett, and McIntosh, *Org. Synth.*, 1955, Coll. Vol. III, p. 237.
[5] Gillam and Stern, "An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," Edward Arnold Ltd., London, 2nd edn., 1957, p. 277.

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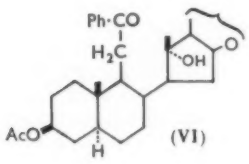
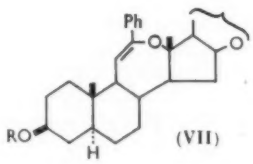
with aqueous acetic acid, the ring opened and 3β-acetoxy-12-phenyl-12,13-seco-5α,25D-spirost-13-en-12-one (VIII) was formed. In contrast, the enol-ether system was unaffected by alkali, which gave the free alcohol (VII; R = H).

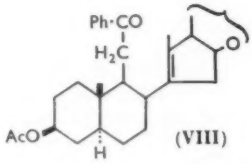
Attempts to oxidise the enol ether (VII; R = Ac) and the phenyl ketone (VIII) with a view to obtaining the lower homologue of hecolic acid were unsuccessful.



(VI)



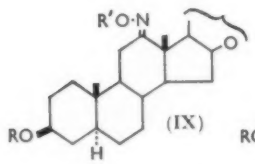
(VII)



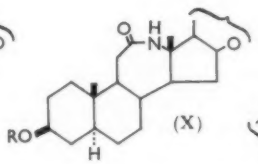
(VIII)

Rearrangement [6] of the oxime [7] (IX; R = Ac, R′ = H) of hecogenin acetate by toluene-*p*-sulphonyl chloride in pyridine yields a lactam (hecololactam), that had been tentatively assigned structure (X; R = Ac) rather than (Xa) on the basis of the ultraviolet spectrum of the related lactam (XIV) derived from 9(11)-dehydrohecogenin acetate oxime (XIII; R = Ac, R′ = H). Since the two isomeric lactones derived from hecogenin were now available, this hypothesis could be tested by conversion of the lactam into the corresponding lactone. According to White,[8] the *N*-nitroso-derivative of a substituted amide or lactam readily loses nitrogen on gentle heating, to yield an ester or lactone. This reaction has already been used successfully in the steroid series by Sato and Latham,[9] in the conversion of *ON*-diacetyldihydrotomatidine and *ON*-diacetyldihydrosolasodine into dihydroneotigogenin and dihydrotigogenin respectively.

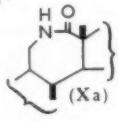
Nitrosation of the lactam acetate (X; R = Ac) by dinitrogen tetroxide in carbon tetrachloride (the reagent used by Sato and Latham) was unselective, attack on the sapogenin side-chain being difficult to control. However, treatment of the lactam acetate in acetic acid and acetic anhydride with sodium nitrite at 0° gave directly (*i.e.*, without isolation of the nitroso-derivative and without heating) hecololactone acetate (II; R = Ac)

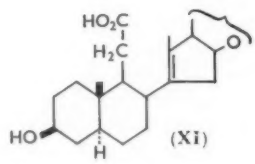


(IX)

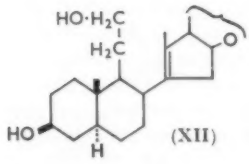


(X)

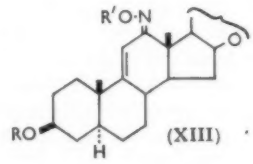

(Xa)



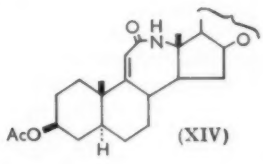
(XI)



(XII)



(XIII)



(XIV)

in 8—10% yield. The material in the mother-liquors failed to crystallise, but methanolic potassium hydroxide and acidification of the solution converted it into a crystalline acid in 90% yield. This is assigned structure (XI), since lithium aluminium hydride reduced it to the known [1] diol (XII). As this acid is derived from hecolic and not isohecolic acid, it

[6] Mazur, *J. Amer. Chem. Soc.*, 1959, **81**, 1454.
[7] Anliker, Rohr, and Heusser, *Helv. Chim. Acta*, 1955, **38**, 1171.
[8] White, *J. Amer. Chem. Soc.*, 1955, **77**, 6008, 6011, 6014.
[9] Sato and Latham, *J. Org. Chem.*, 1957, **22**, 981.

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follows that the lactam must have structure (X). The possibility that the lactam was a mixture is also eliminated.

The oxime (XIII; R = Ac, R′ = H) of 9(11)-dehydrohecogenin acetate was rearranged in an analogous manner to the unsaturated lactam acetate (XIV) (cf. Mazur [6]), but in this case some of the intermediate oxime toluene-*p*-sulphonate (XIII; R = Ac, R′ = *p*-$C_6H_4Me{\cdot}SO_2$) could be isolated. Heating this ester with acidic ethanol converted it into the unsaturated lactam acetate. The unsaturated lactam acetate was recovered unchanged after treatment with sodium nitrite in acetic acid and acetic anhydride.

Experimental

M. p.s were determined on a Kofler block; with certain compounds two m. p.s were observed, with intermediate resolidification; in these cases the first m. p. is enclosed in parentheses below and is only an approximate value. With acids which show this effect the second m. p. is that of the lactone.

Unless otherwise stated, optical rotations were measured for chloroform solutions, and ultraviolet spectra for ethanol solutions. Alumina for chromatography was deactivated by treatment with 10% aqueous acetic acid (5 ml. per 100 g.). Extracts were dried over sodium sulphate before evaporation.

Baeyer–Villiger Oxidation of Hecogenin Acetate.—Hecogenin acetate (100 g.) in chloroform (1·5 l.) and acetic acid (600 ml.) was treated with 30% aqueous hydrogen peroxide (60 ml.) and a 10% v/v solution (40 ml.) of sulphuric acid in acetic acid. The mixture was left for 11 days at room temperature with occasional shaking. The chloroform layer was washed with water several times, mixed with a large volume of water, and steam-distilled until all the solvent was removed. The crude mixture of lactones was filtered off, washed with water, and roughly dried (m. p. 290—295°).

The above mixture was saponified by potassium hydroxide (100 g.) in refluxing methanol (1 l.) and water (100 ml.) for 2 hr. Dilution with water (total volume 3 l.) and filtration afforded neutral material (*A*) (1·9 g.), m. p. 228—230°. The filtrate was acidified with concentrated hydrochloric acid (to Congo Red), and the precipitated acids were filtered off, washed with water, and dried *in vacuo* below 40° [yield, 100 g.; m. p. (197°) 225—258°].

The acids were continuously extracted with hot acetone, and the extracts were concentrated under reduced pressure until crystals formed. These and three further crops obtained by further concentration of the mother-liquors and progressive addition of chloroform, had m. p. (187—203°) 250—254° (82 g.) and were substantially pure hecolic acid. A pure sample of the *hemihydrate* obtained by recrystallisation from acetone–chloroform had m. p. (195°) 260—264°, $[\alpha]_D$ −67·9° (*c* 0·8 in dioxan) (Found, on sample dried at 50°/0·01-mm.: C, 69·0; H, 9·8%; equiv., 470, 473; loss on drying at 105°/0·01 mm., 1·3. $C_{27}H_{44}O_6{\cdot}0{\cdot}5H_2O$ requires C, 68·5; H, 9·6%; equiv., 474; loss on drying, 1·9%), $\nu_{max.}$ (in Nujol) 1724 cm.$^{-1}$ and hydroxyl band. Rothman, Wall, and Eddy [3] record m. p. (187°) 253—255°, $[\alpha]_D$ −66·3° (in dioxan), for the anhydrous material.

The chloroform mother-liquors from the fourth crop, when kept overnight, gave a fifth crop, m. p. (177—200°) 265—270° (5 g.). Recrystallisation from acetone gave 3β,11-*dihydroxy*-11,12-*seco*-5α,25D-*spirostan*-12-*oic acid* (*isohecolic acid*) (IV; R = R′ = H) as prisms, m. p. (239—240°) 285—290° (3·2 g.). A pure sample had m. p. (236—238°) 275—280°, $[\alpha]_D$ −62·9° (*c* 1·02 in dioxan) (Found, on sample dried at room temperature *in vacuo*: C, 69·7; H, 9·8%; Equiv., 465, 468. $C_{27}H_{44}O_6$ requires C, 69·8; H, 9·6%; equiv., 465), $\nu_{max.}$ (in Nujol) 1724 cm.$^{-1}$ and hydroxyl band.

Evaporation of the mother-liquors from the fifth crop gave a solid residue which was dissolved in chloroform and ether and shaken with dilute aqueous potassium hydroxide, the emulsion which was formed being broken by addition of sodium sulphate. The lower aqueous layer was separated, extracted with ether, filtered through kieselguhr, and acidified. The precipitated acid was isolated by two extractions with dichloromethane. Evaporation of the dried extracts and two recrystallisations of the residue from acetone afforded isohecolic acid, m. p. (230—235°) 279—283°, $[\alpha]_D$ −62·6° (*c* 0·78 in dioxan) (600 mg.). The combined chloroform and ether extracts were dried and evaporated to give solid neutral material (*B*) (4·9 g.). Recrystallisation gave material, m. p. 262°, $[\alpha]_D$ −67·7° (*c* 0·95) (Found: C, 72·4; H, 9·6. Calc.

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for $C_{27}H_{42}O_5$: C, 72·6; H, 9·5%). This material is a mixture of lactones, and the infrared spectrum was similar to that of a mixture of hecololactone and isohecololactone. Acetylation gave material of m. p. 293—298°.

Chromatography of the Neutral Material A.—The material (500 mg.) was dissolved in benzene and chromatographed on alumina (50 g.). Elution with ether gave successively (slightly impure) tigogenin, m. p. and mixed m. p. 209—211°, hecogenin, plates, m. p. and mixed m. p. 257—258°, and 12-oxospirost-9(11)-en-3β-ol, m. p. and mixed m. p. 227—230°, $\lambda_{max.}$ 238 mμ (ε 11,400) (cf. Djerassi, Martinez, and Rosenkranz [10]).

Further Treatment of the Neutral Material B.—A portion (2 g.) was refluxed with 10% aqueous potassium hydroxide (10 ml.) in methanol (40 ml.) for 30 min. After dilution with water and filtration from an insoluble fraction (15 mg.; m. p. 292—295°) the solution was extracted with a mixture of benzene, chloroform, and ether. Evaporation of this extract gave material of m. p. 268—275° (40 mg.). The aqueous layer was acidified and the precipitated acids were filtered off and dried [1·78 g.; m. p. (190°) 257—259°]. Six recrystallisations from acetone gave *acid C* (56 mg.), m. p. (214—217°) 254—256°, $[\alpha]_D$ −68·8° (*c* 0·955 in dioxan) (Found: C, 70·3; H, 9·8. $C_{27}H_{44}O_6$ requires C, 69·8; H, 9·6%), $\nu_{max.}$ (in Nujol) 1704 cm.$^{-1}$ and hydroxyl peak. From the mother-liquors from the fourth, fifth, and six crystallisations was obtained a further quantity (171 mg.) of acid C, m. p. (204—208°) 252—261°, $[\alpha]_D$ −69·4° (*c* 1·03 in dioxan). This acid tended to separate as a gel on recrystallisation unless seed-crystals were present.

From the mother-liquors of the first three recrystallisations were obtained, successively, hecolic acid (1·25 g. from chloroform), m. p. (189—193°) 259—265°, and isohecolic acid (121 mg. from acetone), m. p. (230°) 283—285°.

Methyl Isohecolate.—Isohecolic acid with an excess of ethereal diazomethane gave the *methyl ester* (IV; R = H, R′ = Me), needles (from methanol), m. p. (132—134°) 196—198°, $[\alpha]_D$ −55·4° (*c* 0·85) (Found: C, 70·4; H, 9·9. $C_{28}H_{46}O_6$ requires C, 70·3; H, 9·7%), $\nu_{max.}$ (in Nujol) 1724, (in CS_2) 1721 cm.$^{-1}$. With acetic anhydride and pyridine at room temperature overnight this gave the *methyl ester* 3β,11-*diacetate*, prisms (from ether–isopentane), m. p. 117—119°, $[\alpha]_D$ −51·0° (*c* 0·925) (Found: C, 68·5; H, 9·1. $C_{32}H_{50}O_8$ requires C, 68·3; H, 9·0%), $\nu_{max.}$ (in Nujol) 1724, (in CCl_4) 1739 cm.$^{-1}$, no absorption in the hydroxyl region.

Isohecololactone.—Isohecolic acid (250 mg.) was heated to 240°/0·01 mm. It melted, evolved water, and resolidified. The temperature was raised to 260—280°, the lactone then subliming. A second sublimation followed by two recrystallisations from dichloromethane–ether gave 3β,11-*dihydroxy*-11,12-*seco*-5α,25D-*spirostan*-12-*oic acid* 12,11-*lactone* (*isohecololactone*) (V), m. p. 285°, $[\alpha]_D$ −81·3° (*c* 0·96) (Found: C, 72·5, 72·5; H, 9·8, 9·7. $C_{27}H_{42}O_5$ requires C, 72·6; H, 9·5%), $\nu_{max.}$ (in Nujol) 1720, (in CS_2) 1724 cm.$^{-1}$, which with acetic anhydride and pyridine gave the *acetate* (V; R = Ac), needles (from dichloromethane–ether), m. p. (250°) 292—294°, $[\alpha]_D$ −81·1° (*c* 1·3) (Found: C, 71·55; H, 9·1. $C_{29}H_{44}O_6$ requires C, 71·3; H, 9·1%), $\nu_{max.}$ (in Nujol) 1727, (in CS_2) 1739 cm.$^{-1}$, and with benzoyl chloride and pyridine gave the *benzoate*, m. p. 295—297° (from dichloromethane–acetone), $[\alpha]_D$ −75·5° (*c* 0·802) (Found: C, 74·65; H, 8·7. $C_{34}H_{46}O_6$ requires C, 74·15; H, 8·4%), $\nu_{max.}$ (KCl disc) 1724 cm.$^{-1}$.

Derivatives of Hecolic Acid.—The following were made for comparison with the isohecolic acid derivatives: methyl hecolate (III; R = H, R′ = Me), m. p. (78—80°) 163—164°, $[\alpha]_D$ −67° (*c* 1·45), $\nu_{max.}$ (KCl disc) 1724, (in Nujol) 1733 cm.$^{-1}$. Hecololactone (II; R = H), m. p. 259—261° (from dichloromethane–ether), $[\alpha]_D$ −56·5° (*c* 1·29), $\nu_{max.}$ (in Nujol) 1741, (in CS_2) 1736 cm.$^{-1}$. Hecololactone acetate, prisms (from dichloromethane–ether), m. p. (250°) 298—300°, $[\alpha]_D$ −65·0° (*c* 0·98), $\nu_{max.}$ (in Nujol) 1740, (in CS_2) 1739 cm.$^{-1}$. *Hecololactone benzoate*, needles (from dichloromethane–acetone), m. p. 307—310°, $[\alpha]_D$ −63·2° (*c* 0·95) (Found: C, 74·4; H, 8·2. $C_{34}H_{46}O_6$ requires C, 74·2; H, 8·4%), $\nu_{max.}$ (KCl disc) 1739, 1718 cm.$^{-1}$. Methyl hecolate 3-acetate (III; R = Ac, R = Me), m. p. 120—124°, $[\alpha]_D$ −73·2° (*c* 1·34) (Found: C, 69·4; H, 9·7. Calc. for $C_{30}H_{48}O_7$: C, 69·2; H, 9·3%), $\nu_{max.}$ (in Nujol) 1730, (in CCl_4) 1739 cm.$^{-1}$. Except for the last compound these constants are in good agreement with those recorded by Rothman, Wall, and Eddy [3] (cf. methyl hecolate 3-acetate, m. p. 99—101°, $[\alpha]_D$ −62·7°).

Reaction between Methyl Hecolate and Phenylmagnesium Bromide.—Phenylmagnesium bromide was prepared from magnesium turnings (10 g.), bromobenzene (45 ml.), and ether (500 ml.) in the usual way. Methyl hecolate (12 g.) in benzene [600 ml.; dried by distilling off a portion of the solvent (100 ml.)] was added. The mixture was refluxed with stirring for

[10] Djerassi, Martinez, and Rosenkranz, *J. Org. Chem.*, 1951, **16**, 303.

6 hr., then treated with dilute hydrochloric acid and the product was isolated in the usual way by extraction with ether, followed by steam-distillation to remove biphenyl. It gave a yellow froth (12·7 g.), $\lambda_{max.}$ 206 (ε 17,500), 242 mμ (ε 9750), and was treated with pyridine (50 ml.) and acetic anhydride (50 ml.) overnight at room temperature. Working up with ether gave a froth (13·4 g.), $\lambda_{max.}$ 205 (ε 16,000), 242 mμ (ε 9030). This was boiled in acetic acid (25 ml.). After 1 min. a large amount of solid separated. As much as possible of the acetic acid was evaporated under reduced pressure, and the cooled mixture was diluted with di-isopropyl ether (50 ml.). The solid was filtered off, the filtrate evaporated, and the residue treated a second time with boiling acetic acid (10 ml.) to give a second crop of solid. (Weight of first two crops 7·0 g.; m. p. 255—257°.) The material in the mother-liquors was treated a third time with boiling acetic acid, and the material was worked up by dilution with ether and washing with aqueous potassium hydrogen carbonate. Crystallisation of the product from di-isopropyl ether gave a third crop of solid, m. p. 250—252° (0·85 g.). The material in the mother-liquors failed to yield any more solid and had $\lambda_{max.}$ 206 (ε 23,700) and 244 mμ (ε 11,300).

Further crystallisation of the solid gave 3β-*acetoxy*-12-*phenyl*-12a-*oxa*-C-*homo*-5α,25D-*spirost*-11-*ene* (VII; R = Ac) as needles, m. p. 257—259° (from chloroform–methanol), m. p. 254—256° (from dichloromethane–ether), $[\alpha]_D$ −70·5° (*c* 0·64) (Found: C, 76·7; H, 8·6. $C_{35}H_{48}O_5$ requires C, 76·6; H, 8·8%), $\lambda_{max.}$ 205 (ε 11,900), 218 (ε 10,250), 263 mμ (ε 13,100); $\nu_{max.}$ (in Nujol) 1739, 1647, 1605, 1582, 1240, 772 cm.$^{-1}$.

An attempt to isolate the solid product after cyclisation with acetic acid by adding water failed. Solid already formed dissolved on warming and could not be induced to separate again. The amorphous product had $\lambda_{max.}$ 205 (ε 19,700) and 242 mμ (ε 11,350).

3β-*Hydroxy*-12-*phenyl*-12a-*oxa*-C-*homo*-5α,25D-*spirost*-11-*ene* (VII; R = H), obtained by hydrolysis of the acetate with boiling methanolic potassium hydroxide, formed needles (from methanol), m. p. 192—194°, $[\alpha]_D$ −75° (*c* 0·8) (Found: C, 78·6; H, 9·5. $C_{33}H_{46}O_4$ requires C, 78·2; H, 9·15%), $\lambda_{max.}$ 212 (ε 11,300), 263 mμ (ε 13,000), $\nu_{max.}$ (in Nujol) 3390, 1647, 1626, 1605, 1580, 770 cm.$^{-1}$.

The *benzoyl derivative* (benzoyl chloride and pyridine) formed needles (from chloroform–methanol), m. p. 274—277°, $[\alpha]_D$ −76° (*c* 0·6) (Found: C, 78·8; H, 8·5. $C_{40}H_{50}O_5$ requires C, 78·7; H, 8·25%), $\lambda_{max.}$ 214 (shoulder) (ε 18,000), 224 (ε 22,000), 264 mμ (ε 10,400), $\nu_{max.}$ (in Nujol) 1730, 1644, 1608, 1275, 764 cm.$^{-1}$.

Treatment of Methyl Hecolate with Phenyl-lithium.—Methyl hecolate (1 g.) in ether (100 ml.) was refluxed with ethereal 0·78M-phenyl-lithium (15 ml., 6 mol.) for 3 hr. Working up in the usual way (with steam-distillation to remove biphenyl) gave a yellow froth (0·96 g.), $\lambda_{max.}$ 209 (ε 13,000), 242 mμ (ε 8500). A portion of this (50 mg.) was treated with acetic anhydride and pyridine then with boiling acetic acid. The product was chromatographed on alumina, to yield 3β-acetoxy-12a-oxa-12-phenyl-C-homo-5α,25D-spirost-11-ene, m. p. and mixed m. p. 258—260° (eluted with 4 : 1 light petroleum–benzene), and hecololactone acetate, m. p. and mixed m. p. 294—296° (eluted with 1 : 1 light petroleum–benzene).

3β-*Acetoxy*-12-*phenyl*-12,13-*seco*-5α,25D-*spirost*-13-*en*-12-*one* (VIII).—The phenyl enol ether (VII; R = Ac) (501 mg.) was heated on the steam-bath with acetic acid (10 ml.) and water (1 ml.) for 3 hr.; it dissolved except for a trace of amorphous material, which was filtered off. The filtrate was diluted with water and the precipitate filtered off, dissolved in acetic acid, and reprecipitated with water. 3β-*Acetoxy*-12-*phenyl*-12,13-*seco*-5α,25D-*spirost*-13-*en*-12-*one* (VIII) was amorphous and had m. p. 86—91°, $[\alpha]_D$ −40° (*c* 1·175) (Found: C, 76·5; H, 8·9. $C_{35}H_{48}O_5$ requires C, 76·6; H, 8·8%), $\lambda_{max.}$ 206 (ε 20,000), 241 mμ (ε 16,300), $\nu_{max.}$ (KCl disc) 1727 (OAc), 1678 (Ph ketone), 1590 and 1570 (conjugated benzene ring), 1447 (benzene ring), 1239 (OAc), 758, and 697 cm.$^{-1}$ (monosubstituted benzene ring).

Oxidation of the Phenyl Enol Ether (VII; R = Ac) *and of the Phenyl Ketone* (VI).—The following oxidising agents were used in attempts to oxidise the phenyl enol ether (VII; R = Ac): ozone, chromium trioxide in acetic acid, chromium trioxide in aqueous sulphuric acid, potassium permanganate in acetone, osmium tetroxide, perbenzoic acid, and performic acid. In most cases there resulted acidic and neutral fractions from which no crystals were obtained (except benzoic acid, m. p. 120°, formed by chromium trioxide in acetic acid). Oxidation of the crude (acetylated) phenyl ketone (VI), formed by the action of phenyl-lithium on methyl hecolate, with chromium trioxide in acetic acid gave similar results.

Hecogenin Acetate Oxime (IX; R = Ac, R′ = H).—Hecogenin acetate (4·72 g.) and hydroxylamine hydrochloride (2·1 g.) in pyridine (50 ml.) were heated to 90° for 3 hr. Ethanol

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(10 ml.) was added to dissolve the oil, and after 30 min. an excess of water was added. The precipitated solid was filtered off (4·66 g.; m. p. 318—320°). A specimen of this oxime, recrystallised from chloroform–acetone, had m. p. 318—320°, $[\alpha]_D$ −1·7° (*c* 0·785) (Found: C, 71·5; H, 9·0; N, 3·15. Calc. for $C_{29}H_{45}NO_5$: C, 71·4; H, 9·3; N, 2·9%). Mazur [6] recorded m. p. 318—321°, $[\alpha]_D$ −2·4°.

Hecogenin Oxime.—Saponification of the foregoing acetate gave *hecogenin oxime* (IX; R = R = H) as plates (from aqueous methanol), m. p. 256—260°, $[\alpha]_D$ +3° (*c* 1·0) (Found: C, 72·8; H, 9·35; N, 2·9. $C_{27}H_{43}NO_4$ requires C, 72·8; H, 9·7; N, 3·15%). Anliker, Rohr, and Heusser [7] record m. p. 317—318°, $[\alpha]_D$ ±0°, for a hemihydrate prepared in an unspecified manner. Their m. p. is similar to that of the 3β-acetate and the analytical figures quoted are in good agreement with this formulation. Acetylation of hecogenin oxime or its 3β-acetate with acetic anhydride and pyridine at room temperature gave the diacetate (IX; R = R′ = Ac), m. p. 194—196°, $[\alpha]_D$ +16° (*c* 1·1) (Found: C, 70·2; H, 8·7; N, 2·3. Calc. for $C_{31}H_{47}NO_6$: C, 70·3; H, 8·95; N, 2·65%). Anliker *et al.*[7] record m. p. 185°, $[\alpha]_D$ +7·9°.

Hecololactam Acetate.—Hecogenin acetate oxime (2·43 g.) in pyridine (50 ml.) was treated with toluene-*p*-sulphonyl chloride (1·9 g.) at room temperature for 4 days. Water was added till a slight cloudiness appeared, kieselguhr was added, and the solution filtered. Acidificaton of the filtrate precipitated the lactam (2·75 g.) which was isolated by ether-extraction. Crystallisation from aqueous acetone gave 3β-acetoxy-12a-aza-c-homo-5α,25D-spirostan-12-one (hecololactam acetate) (X; R = Ac) as needles, m. p. 234—236°, $[\alpha]_D$ −72·0° (*c* 1·19) (Found: C, 71·62; H, 8·8; N, 3·04. Calc. for $C_{29}H_{45}NO_5$: C, 71·4; H, 9·3; N, 2·9%). If the reaction mixture was worked up after 20 hr. the product consisted of the lactam acetate (1·4 g.) and unchanged oxime (1·03 g.), which were easily separated since the former is only precipitated from aqueous pyridine solution on acidification. Mazur [6] records m. p. 231—234°, $[\alpha]_D$ −70°.

Hecololactam.—The foregoing lactam acetate (500 mg.) in methanol (300 ml.) was refluxed with potassium hydroxide (1·5 g.) in a little water for 2 hr. Addition of an excess of water precipitated 3β-*hydroxy*-12a-*aza*-c-*homo*-5α,25D-*spirostan*-12-*one* (*hecololactam*) (X; R = H) which recrystallised from aqueous methanol as prisms, becoming opaque at 100°, m. p. (150—160°) 202—205°, $[\alpha]_D$ −61·7° (*c* 0·94) (Found, in material dried at 100°/0·01 mm.: C, 70·4; H, 9·5; N, 3·15. $C_{27}H_{43}NO_4,H_2O$ requires C, 69·95; H, 9·8; N, 3·0. Found, in material dried at 132°/0·01 mm.: C, 71·55; H, 9·75. $C_{27}H_{43}NO_4,0·5H_2O$ requires C, 71·4; H, 9·8. Found, in material sublimed at 270—290°/0·01 mm.: C, 72·8; H, 8·25; N, 3·6. $C_{27}H_{43}NO_4$ requires C, 72·8; H, 9·75; N, 3·15%). The sublimed amorphous anhydrous material, on crystallisation from aqueous methanol, gave back the hydrate, m. p. (140—150°) 200—202°. Mazur [6] records that this compound melted over the range 145—215° and gave no analysis.

Action of Nitrous Acid on Hecololactam Acetate.—Hecololactam acetate (1·9 g.) in acetic anhydride (40 ml.) and acetic acid (8 ml.) was cooled to 0° and treated with sodium nitrite (12 g.) for 22 hr. Water was added and the organic material isolated by ether-extraction. This was a syrup which on addition of methanol afforded crystals (140 mg.), m. p. 270—279°. These, after crystallisation from methylene chloride–methanol, gave hecololactone acetate, m. p. 298—301°, $[\alpha]_D$ −63° (*c* 0·79), which did not depress the m. p. of an authentic sample and had an identical infrared spectrum.

The material in the mother-liquors was not crystalline and was refluxed with 5% methanolic potassium hydroxide (50 ml.) for 1 hr. Addition of water caused, on one occasion only, the precipitation of hecololactam, m. p. (145°) 200—205°. In other cases a clear solution was obtained which on acidification with 6N-hydrochloric acid gave crystals (2·1 g.), m. p. 205—215°, $[\alpha]_D$ −37°. Recrystallisation from aqueous acetone gave 3β-*hydroxy*-12,13-*seco*-5α,25D-*spirost*-13-*en*-12-*oic acid* (*anhydrohecolic acid*) (XI), m. p. 220—223°, $[\alpha]_D$ −39° (*c* 1·0) (Found: C, 72·8; H, 9·4. $C_{27}H_{42}O_5$ requires C, 72·6; H, 9·5%), $\lambda_{max.}$ 208 mμ (ε 4450), giving a yellow colour with tetranitromethane in chloroform.

Anhydrohecolyl Alcohol.—(*a*) Anhydrohecolic acid (310 mg.) was treated with lithium aluminium hydride (220 mg.) in refluxing tetrahydrofuran (80 ml.) for 3·25 hr. After decomposition of the excess of reagent and addition of dilute mineral acid the product was isolated by ether. The product (340 mg.), on crystallisation from acetone, gave 12,13-seco-5α,25D-spirost-13-ene-3β,12-diol (anhydrohecolyl alcohol) (XII), m. p. 176—178°, $[\alpha]_D$ −43° (*c* 1·05) (Found: C, 75·25; H, 10·5. Calc. for $C_{27}H_{44}O_4$: C, 74·95; H, 10·25%), $\lambda_{max.}$ 205 mμ (ε 4400).

(*b*) Hecolyl alcohol, prepared by reduction of methyl hecolate with lithium aluminium

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hydride in tetrahydrofuran,[2] had m. p. 140—142°, $[\alpha]_D$ −65° (*c* 0·8 in acetone). Rothman *et al.*[2] record m. p. 141°, $[\alpha]_D$ −71·4°.

This material (100 mg.) was dissolved in methanol (5 ml.) and treated with 60% aqueous perchloric acid (0·1 ml.) at 20° for 17 hr. Addition of water precipitated anhydrohecolyl alcohol, m. p. 178—181° undepressed by admixture with material prepared by method (*a*) and having an identical infrared spectrum. Rothman *et al.*[2] record m. p. 174—176°, $[\alpha]_D$ −46·1°.

9(11)-*Dehydrohecogenin Acetate Oxime*.—9(11)-Dehydrohecogenin acetate [10] was converted into its oxime (XIII; R = Ac, R′ = H) by the method used for hecogenin acetate. It had m. p. 286—289°, $[\alpha]_D$ +26°, $\lambda_{max.}$ 238 mμ (ε 11,000). Mazur [6] records m. p. 282—284°, $[\alpha]_D$ +36°, $\lambda_{max.}$ 238 mμ (ε 13,600).

Beckmann Rearrangement of 9(11)-*Dehydrohecogenin Acetate Oxime*.—The oxime (5·18 g.) in pyridine (80 ml.) was treated with toluene-*p*-sulphonyl chloride (4 g.) at 20° for 64 hr. Water (1 l.) was added and the precipitated pink solid filtered off (m. p. 168—175°; 3·55 g., 52%). Crystallisation from aqueous acetone gave needles of 12-*toluene*-p-*sulphonyloxyimino*-5α,25D-*spirost*-9(11)-*en*-3β-*yl acetate* (XIII; R = Ac, R′ = *p*-$C_6H_4Me{\cdot}SO_2$), m. p. 184—186°, $[\alpha]_D$ −46° (*c* 1·46) (Found: C, 67·1; H, 7·4; N, 2·3; S, 5·1. $C_{36}H_{49}NO_7S$ requires C, 67·6; H, 7·7; N, 2·2; S, 5·0%), $\lambda_{max.}$ 204 (ε 21,000), 227 mμ (ε 21,600), $\nu_{max.}$ (KCl disc) 3422, 1736, 1666, 1629, 1600, 1250 cm.$^{-1}$.

The aqueous pyridine filtrates were acidified to pH 3 with hydrochloric acid, and the precipitate filtered off (m. p. 220—227°; 2·2 g., 40%). Recrystallisation from aqueous acetone gave 3β-acetoxy-12a-aza-c-homo-5α,25D-spirost-9(11)-en-12-one (dehydrohecololactam acetate), m. p. 230—232°. From acetone–light petroleum (b. p. 60—80°) it separated as prisms, m. p. 255—258°, $[\alpha]_D$ −69·4° (*c* 1·19) (Found: C, 71·5; H, 9·2; N, 3·0. Calc. for $C_{29}H_{43}NO_5$: C, 71·7; H, 8·9; N, 2·9%), $\lambda_{max.}$ 220 mμ (ε 17,200). There was no loss in weight at 100°/0·01 mm. The two forms of this substance had identical infrared spectra. Mazur [6] records m. p. 228—231°, $[\alpha]_D$ −72°, $\lambda_{max.}$ 220 mμ (ε 15,800).

Treatment of Dehydrohecololactam Acetate with Nitrous Acid.—The lactam acetate (206 mg.) in acetic anhydride (4 ml.) and acetic acid (0·8 ml.) was treated with sodium nitrite (1·1 g.) at 0° for 68 hr. Addition of water and extraction with ether gave neutral material (200 mg.). Crystallisation from acetone–light petroleum gave the starting material, m. p. and mixed m. p. 254—257° (60 mg.). Further crops (total 120 mg.) had m. p. 252—255°.

Formation of Dehydrohecololactam Acetate from the Oxime Toluene-p-*sulphonate* (XIII; R = Ac, R′ = *p*-$C_6H_4Me{\cdot}SO_2$).—(*a*) The oxime toluene-*p*-sulphonate (160 mg.) in ethanol (8 ml.), acetic acid (4 ml.), and a few drops of water was refluxed for 30 min. Addition of water precipitated the lactam acetate which after crystallisation from acetone–light petroleum had m. p. 252—255°.

(*b*) On attempted recrystallisation of the oxime toluene-*p*-sulphonate (3·5 g.) from chloroform–methanol, a syrup was obtained. Prolonged storage of this in ether–isopentane gave the low-melting form of the lactam acetate (1·5 g.), m. p. 222—226°.

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680. *Complex Halides of the Transition Metals. Part II.*[1] *Tetrahedral Iron Complexes.*

By NAIDA S. GILL.

The preparation of complex halides of the type $R_2[Fe^{II}Hal_4]$, where $R = [Et_4N]^+$ or $[Ph_3MeAs]^+$ and Hal = Cl, Br, or I, is reported. Conductivity, spectra, magnetic susceptibility, and crystal structure have been studied and comparison with those of similar complexes of other bivalent transition metals leads to the conclusion that $[Fe^{II}Hal_4]^{2-}$ ions have a tetrahedral structure. Spectra of $[Fe^{III}Cl_4]^-$ and $[Fe^{III}Br_4]^-$ are also reported.

CRYSTAL-FIELD theory predicts that spin-free Fe^{II} with six *d*-electrons will form tetrahedral complexes in which the ground state has the electronic configuration $d_\gamma^3 d_\epsilon^3$. The unsymmetrical filling of the d_γ-sub-level in such an arrangement of non-bonding electrons is expected to lead to slight distortion from a regular tetrahedral structure. However, if the ligand-field effects are of major importance in determining the stereochemistry of an Fe^{II} complex, then the crystal-field stabilisation energy will favour the formation of octahedral complexes rather than tetrahedral ones, although the difference in stabilisation is only small, being of the order of 3 kcal. mole^{-1}. In accordance with this prediction the existence of tetrahedral complexes of Fe^{II} has not yet been proved although recently complexes with triphenylphosphine [2,3] and triphenylarsine [2] have been described and this structure has been proposed for them. These complexes are of two types. The first are non-electrolytes of formula $FeX_2,2PPh_3$, where X = Cl, Br, or I, similar to the compounds $NiX_2,2PPh_3$ which have been shown to be tetrahedral in structure although greatly distorted.[4] The second are electrolytes which appear to contain the cations $[Fe(PPh_3)_4]^{2+}$ and $[Fe(AsPh_3)_4]^{2+}$, and the compound of empirical formula $FeI_2,2AsPh_3$, which is ionic in nitrobenzene solution, so that a possible structure is $[Fe(AsPh_3)_4][FeI_4]$.

TABLE 1. *Properties of tetrahalogeno-complexes of* Fe^{II}.

Compound	μ_{eff} at 20° (B.M.)	Molar conductivity in $Ph{\cdot}NO_2$ at 25°	Compound	μ_{eff} at 20° (B.M.)	Molar conductivity in $Ph{\cdot}NO_2$ at 25°
$[Ph_3MeAs]_2[FeCl_4]$ ...	5·33	58 (c = 0·0005M)	$[Et_4N]_2[FeBr_4]$ ...	5·46	—
$[Et_4N]_2[FeCl_4]$	5·40	—	$[Ph_3MeAs]_2[FeI_4]$...	5·40	53 (c = 0·001M)

In Part I [1] the preparation and properties of tetrahedral nickel halide complexes of the type $R_2[M^{II}Hal_4]$, where $R = [Et_4N]^+$ or $[Ph_3MeAs]^+$ and Hal = Cl, Br, or I, were described and the factors which influence the stereochemistry of complex ions discussed. It was shown that not only are ligand-field effects of importance in determining stereochemistry of complexes but also those arising from covalent bonding. Thus in circumstances favourable to the stability of the ions $[MHal_4]^{2-}$, *e.g.*, lowering of the solvation energy of the metal ion, such tetrahedral ions can be formed with certain bivalent metals of the first transition series and compounds containing them have been isolated. In this way, by using ethyl alcohol as solvent, salts of the anions $[FeHal_4]^{2-}$ have been prepared. The cations $[Et_4N]^+$ and $[Ph_3MeAs]^+$ were used but it was not possible to obtain each tetrahalogeno-complex with both; *e.g.*, $[Et_4N]_2[FeI_4]$ could not be prepared by the above method, only tetraethylammonium iodide crystallising from a mixture of this salt and ferrous iodide in ethyl alcohol. This was due, presumably, to the relative lattice energies of the required complex salt and tetraethylammonium iodide and the stability of the complex anion.

In Table 1 are given the properties of the compounds which have been prepared. All

[1] Part I, Gill and Nyholm, *J.*, 1959, 3997.
[2] Naldini, *Gazzetta*, 1960, **90**, 361.
[3] Hieber and Floss, *Z. anorg. Chem.*, 1957, **291**, 314.
[4] Venanzi, *J.*, 1958, 719; Powell and Venanzi, *Proc. Chem. Soc.*, 1956, 6.

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form cream-coloured crystals, and *X*-ray studies have shown that the arsonium salt of $[FeCl_4]^{2-}$ is isomorphous with those of $[MnCl_4]^{2-}$, $[MnBr_4]^{2-}$, $[CoCl_4]^{2-}$, $[CoBr_4]^{2-}$, $[NiCl_4]^{2-}$, and $[ZnCl_4]^{2-}$ as reported in Part I [5] and that the tetraethylammonium salt is isomorphous with those of $[MnCl_4]^{2-}$ and $[NiCl_4]^{2-}$, showing that $[FeCl_4]^{2-}$ is tetrahedral in the same way as these reference ions have been shown to be.[1,5] Similarly the tetraethylammonium salt of $[FeBr_4]^{2-}$ is isomorphous with that of $[MnBr_4]^{2-}$. The arsonium salt of $[FeI_4]^{2-}$ crystallises in leaflets as do the isomorphous series $[MnI_4]^{2-}$, $[CoI_4]^{2-}$, $[NiI_4]^{2-}$, $[ZnI_4]^{2-}$.[1] The crystal properties of the $[FeHal_4]^{2-}$ salts therefore undoubtedly show that these complex anions are all tetrahedral and a detailed study of them will be reported later by Dr. P. J. Pauling.

While the magnetic moments of bivalent iron complexes cannot be expected to prove their stereochemistry they are of interest. Fe^{2+} has a $^5D_4$ ground state which under the influence of the cubic field of a tetrahedral arrangement of ligands splits into a lower non-magnetic doublet (^5E) and an upper triplet ($^5T_2$), so that magnetic behaviour similar to that of octahedral Cu^{II} is to be expected.[6,7] Thus only a small orbital contribution to the magnetic moment above that of the spin-only value of 4·90 B.M. is predicted for a near-regular tetrahedral complex. The μ_{eff} values given in Table 1 show that the moments at room temperature are high even when " mixing-in " of the first excited level by spin–orbit

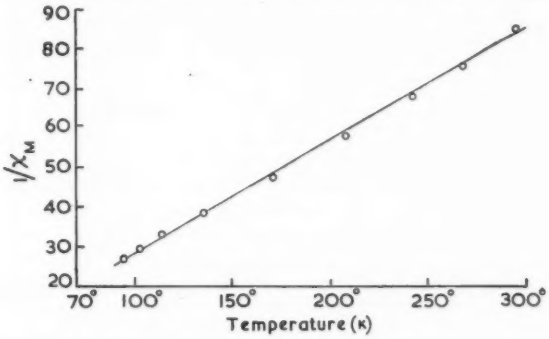

FIG. 1. *Plot of* $1/\chi_M$ *against temperature for* $[Et_4N]_2[FeCl_4]$.

coupling is allowed for by the formula $\mu = \mu_0 (1 - 2\lambda/\Delta)$, provided reasonable assumptions are made for the values of λ and Δ, of the order of -80 and 3000 cm.$^{-1}$, respectively, giving $\mu_{eff} = \sim 5{\cdot}20$ B.M. The moment of $[FeCl_4]^{2-}$ in the tetraethylammonium salt has been measured over the temperature range $-178°$ to $+22°$, giving a θ value of zero; the plot of magnetic susceptibility against temperature is shown in Fig. 1.

It is also to be expected that there would be an increase in the magnetic moment in the order Cl < Br < I, as Δ decreases in this order and so increases the spin–orbit coupling. No trend of this kind was observed, the moments of the three complex ions being within the range of experimental error at room temperature. This seems to exclude an explanation of the high magnetic moments in terms of contribution from the $^5T_2$ triplet. Since spectroscopic measurements showed that there could be no more than traces of Fe^{III} complexes present in these Fe^{II} compounds, the only explanation of the high magnetic moments could be behaviour intermediate between that of tetrahedral Fe^{II} and that of the field-free Fe^{2+} ion. If the ligand field due to the halide ions were extremely weak it is feasible that the Fe^{II} atom would tend a little towards behaving as a field-free Fe^{2+} ion, for which the magnetic moment, calculated from the formula, $\mu = g\sqrt{J(J+1)}$, is 6·67 B.M., and the moment of the $[FeX_4]^{2-}$ would thus be raised above the value predicted by theory for a tetrahedral complex.

[5] Porai-Koshits, *Kristallografiya*, 1956, **1**, 291; Brehler, *Z. Krist.*, 1957, **109**, 68.
[6] Van Vleck, *Phys. Rev.*, 1932, **41**, 208.
[7] Figgis and Harris, *J.*, 1959, 855.

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The conductivities of the $[FeCl_4]^{2-}$ and $[FeI_4]^{2-}$ salts show that they are uni-bivalent electrolytes in nitrobenzene, as expected. However, some dissociation of $[FeI_4]^{2-}$ must occur in organic solvents as the solutions have the characteristic dark colour of ferrous iodide in such solvents, presumably owing to formation of free iodine, although the conductivity in nitrobenzene shows that dissociation cannot occur to any large extent in that solvent.

FIG. 2. *Absorption spectra of* (1) $[FeCl_4]^{2-}$ (0·05M), (2) *as* (1) *but with* $10^{-1}\varepsilon$, (3) $[FeCl_4]^{-}$ (0·1M), *and* (4) *as* (3) *but with* $10^{-1}\varepsilon$, *all in dimethylformamide.*

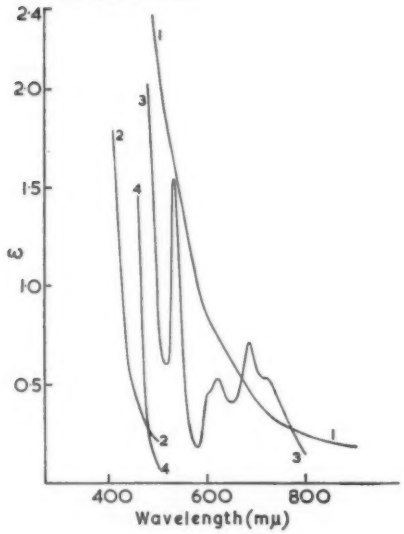
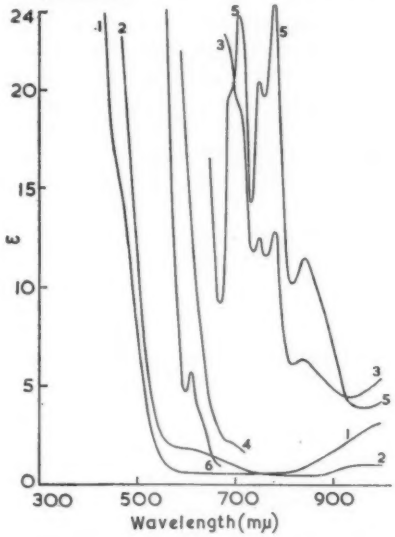


FIG. 3. *Absorption spectra of* (1) $[FeBr_4]^{2-}$ (0·01M), (2) *as* (1) *but with added* Br^-, (3) $[FeBr_4]^{-}$ (0·006M), (4) *as* (3) *but with* $10^{-1}\varepsilon$, (5) *as* (3) *but with added* Br^-, *and* (6) *as* (5) *but with* $10^{-1}\varepsilon$, *all in dimethylformamide.*



The spectra of $[FeCl_4]^{2-}$ and $[FeBr_4]^{2-}$* were measured in deoxygenated dimethylformamide and compared with those of $[FeCl_4]^{-}$ and $[FeBr_4]^{-}$ in the same solvent. The effect on the spectra of the addition of excess of halide ions necessary to obtain a constant

TABLE 2. *Spectra of tetrahalogeno-complexes of* Fe^{III} *in the visible region.*

Ion	$\varepsilon_{max.}$	$\lambda_{max.}$	Concn. of soln. in H·CO·NMe_2 (M)	Ion	$\varepsilon_{max.}$	$\lambda_{max.}$	Concn. of soln. in H·CO·NMe_2 (M)
$[FeCl_4]^-$	0·53	722	0·1				
	0·72	685					
	0·52	620					
	(sh.)	607					
	1·54	533					
$[FeBr_4]^-$	6·3	835	0·006	$[FeBr_4]^-$ +	11·4	844	0·006
	12·8	779		excess Br^-	24·0	779	
	12·4	750			20·4	752	
	(sh.)	713			23·7	713	
	(sh.)	684			(sh.)	688	
					57·3	608	

value of ε was also studied; the observed results are shown in Fig. 2 and the values of $\varepsilon_{max.}$ and $\lambda_{max.}$ given in Table 2. In the spectrum of the octahedral hexa-aquo-complex of Fe^{2+} one band occurs at 10,400 $cm.^{-1}$ and three much weaker ones at 19,800—25,900 $cm.^{-1}$.[8] The former has been assigned to the transition $^5T_2 \longrightarrow {}^5E$ and thus in tetrahedral complexes of Fe^{II} the *d–d* band can be expected at long wavelengths well outside the visible

* As the tetraethylammonium salts.

[8] Jørgensen, *Acta Chem. Scand.*, 1954, **8**, 1502.

region. Examination of the spectrum of $[FeCl_4]^{2-}$ between 10,000 and 7000 cm.$^{-1}$ (in solution) and between 7800 and 3000 cm.$^{-1}$ in a Nujol mull showed that this transition occurs below 3000 cm.$^{-1}$. The other bands of $[Fe(H_2O_6)]^{2+}$ have not been definitely assigned because the energy levels of the ^3P, ^3H, and ^3F states are very close together. In the case of the tetrahedral complexes very intense charge-transfer bands occur beyond 20,000 cm.$^{-1}$; as large dilutions are necessary to measure them in solution it is considered that the results obtained are unlikely to be meaningful and they are not included in this paper.

Comparison of the spectra of the Fe^{II} complexes with those of the Fe^{III} complexes shows that the former are not oxidised in solution. Within the wavelength range studied halide ions had little or no effect on the spectra of $[FeCl_4]^{2-}$, $[FeBr_4]^{2-}$, and $[FeCl_4]^-$, but had considerable effect on that of $[FeBr_4]^-$. The lack of change produced in the spectra of the former ions and the increase in $\varepsilon_{max.}$ in that of the last are taken to indicate that no significant concentration of $[MX_6]^{x-}$ is formed under these conditions, as this should considerably decrease the value of the extinction coefficient. The change in the spectrum of $[FeBr_4]^-$ must then be due either to solvation of the complex ion or to displacement of Br^- by dimethylformamide, which is at least partially counteracted by the addition of excess of halide ions. The spectrum of $[FeBr_4]^-$ has not previously been reported; that of $[FeCl_4]^-$ in diethyl ether [9] and in di-isopropyl ether [10] has been studied but not interpreted. The spectra of $[FeCl_4]^-$ in these solvents and in dimethylformamide are very similar except that the band observed at 500 mμ in the ethers does not appear in dimethylformamide solution. A discussion of the spectra of both the chloro- and the bromo-complexes of Fe^{III} will be published by Dr. T. M. Dunn.

Experimental

Preparation of Ferrous Compounds.—All were prepared by mixing, in an atmosphere of nitrogen, fairly concentrated solutions of the calculated amounts of the appropriate ferrous halide and triphenylmethylarsonium or tetraethylammonium halide in ethyl alcohol which had been boiled to remove oxygen. The products crystallised immediately and no precautions to prevent oxidation of the chloro- and bromo-compounds were necessary if filtration was rapid. For the iodo-compound it was necessary to carry out all work in nitrogen. None of the compounds was recrystallised as decomposition occurred in hot alcohol. Thus were obtained: *bis(triphenylmethylarsonium) tetrachloroferrate*(II), cream needles stable to oxidation when dry (Found: C, 54·0; H, 4·6; Cl, 17·1. $C_{38}H_{36}As_2Cl_4Fe$ requires C, 54·3; H, 4·3; Cl, 16·9%); *bis(tetraethylammonium) tetrachloroferrate*(II), cream needles stable to oxidation when dry (Found: C, 42·4; H, 8·2. $C_{16}H_{40}Cl_4FeN_2$ requires C, 42·0; H, 8·8%); *bis(tetraethylammonium) tetrabromoferrate*(II), cream needles stable to oxidation when dry (Found: C, 30·2; H, 6·4. $C_{16}H_{40}Br_4FeN_2$ requires C, 30·0; H, 6·3%); *bis(triphenylmethylarsonium) tetraiodoferrate*(II), cream leaflets readily oxidised in air (Found: C, 38·1; H, 3·5; I, 41·1. $C_{38}H_{36}As_2FeI_4$ requires C, 37·9; H, 3·0; I, 42·2%).

Preparation of Ferric Compounds.—These were prepared in the same way as those of Fe^{II} except that no precautions against oxidation were necessary. Recrystallisation from ethyl alcohol gave *bis(tetraethylammonium) tetrachloroferrate*(III), yellow needles (Found: C, 29·8; H, 6·4. $C_8H_{20}Cl_4FeN$ requires C, 29·3; H, 6·1%), and *tetrabromoferrate*(III), brown needles (Found: C, 19·1; H, 4·2; Br, 63·2. $C_8H_{20}Br_4FeN$ requires C, 18·9; H, 4·0; Br, 63·2%).

Absorption Spectra.—Solutions of the Fe^{II} complexes were prepared by direct distillation, under nitrogen, of dimethylformamide into the cell containing a known weight of the compound. The spectra were obtained with a Unicam S.P. 500 spectrophotometer.

Magnetic susceptibilities were determined by the Gouy method.[11]

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[9] Friedman, *J. Amer. Chem. Soc.*, 1952, **74**, 5.
[10] Metzler and Myers, *J. Amer. Chem. Soc.*, 1950, **72**, 3776.
[11] Figgis and Nyholm, *J.*, 1959, **331**.

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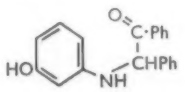
681. 4- *and* 6-*Hydroxy*-2,3-*diphenylindole and* 2,3-*Diphenylindole*-4,7- *and* -6,7-*quinone.*

By Barbara Clifford, Patricia Nixon, Charlotte Salt, and Muriel Tomlinson.

An earlier report [1] that the compound, m. p. 168°, formed by reaction between *m*-aminophenol and benzoin, is 6- and not 4-hydroxy-2,3-diphenylindole, has been proved to be correct in spite of a claim [2] to the contrary. The quinone formed by oxidation of the 6-hydroxy-compound is now shown to be 2,3-diphenylindole-6,7-quinone, and not, as was claimed,[2] the 4,7-quinone. The latter compound has been prepared by oxidation of both 4-hydroxy- and 4,7-dihydroxy-2,3-diphenylindole, which proves its constitution.

Teuber and Schnee [2] disagreed with the findings of Orr and Tomlinson [1] who showed that the compound, m. p. 168°, made by cyclisation of *m*-*N*-(α-phenylphenacyl)aminophenol (I) was 6- (II; R = OH, R′ = H) and not 4-hydroxy-2,3-diphenylindole (III; R = OH, R′ = H). They repeated Orr and Tomlinson's work and claimed that removing the chlorine from 7-chloro-4-methoxy-2,3-diphenylindole (III; R = OMe, R′ = Cl) gave a methoxydiphenylindole, m. p. 202°, identical with the compound obtained either by methylating the substance, m. p. 168°, or from *m*-anisidine and benzoin. This led us to repeat our experiments.



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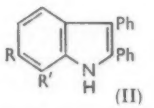

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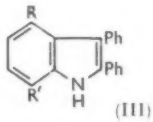


(III)

We prepared our 2-chloro-5-methoxyaniline from *p*-anisidine (acetylation, nitration, and hydrolysis, followed by conversion of the resulting 4-methoxy-2-nitroaniline into the amine by the Sandmeyer reaction and reduction). There is therefore no doubt about the constitution of this amine, or of the 7-chloro-4-methoxy-2,3-diphenylindole (III; R = OMe, R′ = Cl) obtained from it by condensation with benzoin. (Attempts to make this indole from deoxybenzoin 2-chloro-5-methoxyphenylhydrazone failed.) Removal of the chlorine now gave 4-methoxy-2,3-diphenylindole (III; R = OMe, R′ = H), m. p. 147—148°, and demethylation afforded 4-hydroxy-2,3-diphenylindole (III; R = OH, R′ = H), m. p. 149·5—151°, quite different from the 6-methoxy- and the 6-hydroxy-compound, m. p. 203° and 168°, respectively.

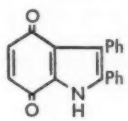
There is some evidence to support these structures in their very complex infrared spectra: the 6-methoxy-compound has maxima at 864, 834, and 812 cm.$^{-1}$ which are absent in the spectrum of the 4-methoxy-compound and could be attributed to the out-of-plane bending of one isolated, and two adjacent, hydrogen atoms on the benzenoid ring of the indole. Ockenden and Schofield [3] have, moreover, shown that 6- rather than 4-substituted indoles are normally obtained from phenylhydrazones which have strongly *ortho*- and *para*-directing substituents *meta* to the hydrazino-group, and they obtained only a substance, m. p. 204—207°, from deoxybenzoin *m*-methoxyphenylhydrazone.

It seemed possible that the discrepancies between the German authors' results and our own was a mistake about the identity of their starting material, namely, the 4-chloro-3-nitroanisole, which was a gift to them from Farbenwerken Hoechst A.G., and as a partial check on this we prepared a methoxydiphenylindole from *o*-anisidine (the most likely alternative if such a mistake had occurred). By a series of operations similar to those described for *p*-anisidine, we did obtain 6-methoxy-2,3-diphenylindole, m. p. 203°, but the

[1] Orr and Tomlinson, *J.*, 1957, 1025.
[2] Teuber and Schnee, *Ber.*, 1958, **91**, 2089.
[3] Ockenden and Schofield, *J.*, 1957, 3175.

melting point of the intermediate 5-chloro-6-methoxy-2,3-diphenylindole did not correspond with that of Teuber and Schnee's chloromethoxydiphenylindole.

These authors did not quote the melting point of their chloromethoxyaniline [its hydrochloride had m. p. 208° (decomp.); ours, m. p. 213—214° (decomp.)] but they made it by catalytic reduction in an autoclave at 80° and our experience shows that it could, therefore, have been contaminated with *m*-anisidine. In addition we have found that during the cyclisation of 2-chloro-5-methoxy-*N*-(α-phenylphenacyl)aniline, some chlorine is always extruded. We worked with analytically pure 2-chloro-5-methoxyaniline and yet we could isolate, from the product, 6-methoxy-2,3-diphenylindole which could not have arisen from *m*-anisidine in the starting material. Teuber and Schnee did not recrystallise their 7-chloro-4-methoxy-2,3-diphenylindole (it was distilled *in vacuo*). It could therefore have been contaminated with 6-methoxy-2,3-diphenylindole from either or both of the above sources, and, if it was, this very sparingly soluble compound would be isolated far more easily than the 4-isomer, after the dechlorination experiment: their yield was only 28%. (We can obtain an 84% yield of the 4-methoxy-compound.)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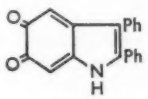
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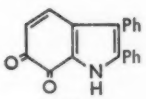
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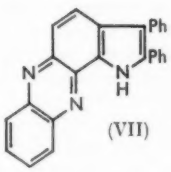
(VII)

Teuber and Schnee oxidised the hydroxy-2,3-diphenylindole, m. p. 168°, with potassium nitrosodisulphonate (Frémy's salt) and obtained a quinone, m. p. 235°, which they claim is 2,3-diphenylindole-4,7-quinone (IV). We have synthesised this quinone by demethylation and oxidation (sodium dichromate) of 4,7-dimethoxy-2,3-diphenylindole. Its infrared absorption spectrum is identical with that of the quinone which we got by oxidation of 4-hydroxy-2,3-diphenylindole with Fremy's salt.

Similar oxidation of 6-hydroxy-2,3-diphenylindole, which had been purified through the sodium salt or by conversion into the 6-methoxy-compound, gave a quinone which did not melt completely below 320°. Oxidation of 6-hydroxydiphenylindole which had been " purified " chromatographically gave this quinone, together with a small quantity of the above 4,7-quinone. The isolation of the 4,7-quinone here was our first indication that 4-hydroxy-2,3-diphenylindole is formed, together with the 6-isomer, from *m*-aminophenol and benzoin. We find now, however, that when the product of this reaction is methylated and chromatographed a little of the 4-methoxy-compound can be isolated from the first fractions.

The new quinone is an *o*-quinone because it forms a phenazine with *o*-phenylenediamine, and it must be either 2,3-diphenylindole-5,6- (V) or 2,3-diphenylindole-6,7-quinone (VI). Oxidation of 6-hydroxy-1-methyl-2,3-diphenylindole also gave an *o*-quinone which yielded a phenazine identical with that obtained by methylating the phenazine (VII). The infrared spectra of the quinone from 6-hydroxydiphenylindole, and of the phenazine derived from it, both contain a wide band at 2900—3400 cm.$^{-1}$, and this band is absent from the spectra of the corresponding *N*-methyl compounds. The hydrogen-bonding thus indicated suggests that these substances are 2,3-diphenylindole-6,7-quinone (VI) and 4′,5′-diphenylpyrrolo(2′,3′:1,2)phenazine (VII) respectively, because, although both indole-6,7-quinones and indole-5,6-quinones (in the imino-form) could be hydrogen-bonded, the phenazine from an indole-5,6-quinone is incapable of forming hydrogen bonds.

Teuber and Schnee stated that their quinone from the hydroxyindole, m. p. 168°, does not form a phenazine but gives, with *o*-phenylenediamine, a " dianil," m. p. 318—320°. We obtained the compound they describe (working under their conditions in pyridine), but the main product is the phenazine (VII) which they must have removed by washing

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the " dianil " with boiling benzene. The identity of this substance has not been established. It is not, as they suggest, 2,3-diphenylindole-4,7-quinone *oo'*-diaminodianil because the 4,7-quinone does not form this substance with *o*-phenylenediamine. The analysis accords with a formula, $C_{32}H_{23}N_5$, rather better than with the dianil formula, and the compound might have been formed by addition of *o*-phenylenediamine across the 4,5-double bond of the quinone (VI) followed by some oxidation: it is not formed when the phenazine (VII) is boiled with *o*-phenylenediamine in pyridine. It does not react with acetic anhydride and it is therefore unlikely that it contains an NH_2 group.

Experimental

6- *and* 4-*Methoxy*-2,3-*diphenylindole*.—*m*-Aminophenol (6 g.) and benzoin (5 g.) were converted into the indole [1] and the resulting gum, in benzene, was chromatographed on 5% deactivated alumina. Fractions collected from a wide grey band (mauve fluorescence) contained solids, m. p. 155—163°. This material (5·7 g.) was methylated,[1] dissolved in a minimum volume of benzene and chromatographed on activated alumina in benzene. A small quantity of gum in the first fraction gave, on recrystallisation from light petroleum (b. p. 60—80°), prisms, m. p. 136—140°, raised to 142° by admixture with 4-methoxy-2,3-diphenylindole, m. p. 146—147°. Later fractions gave the 6-methoxy-compound.

2-*Chloro*-5-*methoxyaniline*.—The corresponding nitro-compound has been reduced in various ways but the original method [4] produces the purest amine. Steam-distillation facilitates its isolation.

2-*Chloro*-5-*methoxyphenylhydrazine*.—The above amine (10 g.) was diazotised in hydrochloric acid (20 ml.) and water (25 ml.) with sodium nitrite (4·6 g.). The diazonium solution was reduced with stannous chloride (36 g.) in hydrochloric acid (50 ml.), and the *hydrazine* was liberated from the precipitated hydrochloride with sodium hydroxide. It separated from light petroleum (b. p. 60—80°) as needles, m. p. 70—72·5° (3·0 g.) (Found: C, 48·5; H, 5·1. $C_7H_9ClN_2O$ requires C, 48·6; H, 5·2%). When warmed with deoxybenzoin it gave *deoxybenzoin* 2-*chloro*-5-*methoxyphenylhydrazone*, needles, m. p. 100—101° (from methanol) (Found: C, 72·0; H, 5·4. $C_{21}H_{19}ClN_2O$ requires C, 72·0; H, 5·4%).

2-*Chloro*-5-*methoxy*-N-(α-*phenylphenacyl*)*aniline* has now been obtained in a second form, m. p. 116° (Found: C, 71·6; H, 5·0. $C_{21}H_{18}ClNO_2$ requires C, 71·4; H, 5·1%).

7-*Chloro*-4-*methoxy*-2,3-*diphenylindole*.—This was prepared as described earlier [1] from 2-chloro-5-methoxy-*N*-(α-phenylphenacyl)aniline (3·0 g.) and 2-chloro-5-methoxyaniline hydrochloride (1·5 g.), both made from 2-chloro-5-methoxyaniline (4·78 g.) (Found: C, 53·5; H, 5·2. Calc. for C_7H_8ClNO: C, 53·3; H, 5·2%). Chromatography of the reaction product in benzene on activated alumina gave, first, a yellow band which contained the chloromethoxyindole and some αβ-di-(2-chloro-5-methylanilino)stilbene. A second red band yielded a gum which, in contact with methanol, gave a solid, m. p. 190—192° (0·425 g.), and this, recrystallised from methanol, afforded 6-methoxy-2,3-diphenylindole, m. p. 200°.

5-*Chloro*-6-*methoxy*-2,3-*diphenylindole* was obtained from 4-chloro-3-methoxyaniline (1·0 g.) and benzoin (1·3 g.) heated with a little hydrochloric acid at 200° for 1 hr., as plates, m. p. 217° (from ethanol) (Found: C, 75·7; H, 5·0. $C_{21}H_{16}ClNO$ requires C, 75·6; H, 4·8%). When this was reduced with hydrogen and palladium–charcoal in mesitylene (cf. ref. 1) it gave 6-methoxy-2,3-diphenylindole.

4-*Hydroxy*-2,3-*diphenylindole*.—The 4-methoxy-compound (1·6 g.) in dry benzene (40 ml.) with aluminium chloride (5·0 g.) was heated under reflux in nitrogen for 8 hr. Ice and hydrochloric acid were added; 4-*hydroxy*-2,3-*diphenylindole* was isolated with ether and recrystallised from light petroleum (b. p. 60—80°) as prisms, m. p. 149—151·5° (0·41 g.) (Found: C, 84·2; H, 5·4. $C_{20}H_{15}NO$ requires C, 84·2; H, 5·3%). Methylation in aqueous acetone reconverted it into the 4-methoxy-compound.

7-*Chloro*-4-*hydroxy*-2,3-*diphenylindole* (0·78 g.) was made the same way from the corresponding methoxy-compound (1·2 g.). It formed plates, m. p. 174—175° (from light petroleum b. p. 80—100°) (Found: C, 75·1; H, 4·7. $C_{20}H_{14}ClNO$ requires C, 75·1; H, 4·4%.)

4,7-*Dimethoxy*-2,3-*diphenylindole*.—Heated together at 150—160°, with a drop of hydrochloric acid, 2,5-dimethoxyaniline (2·5 g.) and benzoin (3·5 g.) gave a gum which, chromatographed on activated alumina in benzene, yielded 2,5-*dimethoxy*-N-(α-*phenylphenacyl*)*aniline*,

[4] Cummins and Tomlinson, *J.*, 1955, 3475.

prisms, m. p. 91—92° (from ethanol) (Found: C, 76·1; H, 6·2; N, 4·0. $C_{21}H_{21}NO_3$ requires C, 76·1; H, 6·1; N, 4·0%). This (1·55 g.), with 2,5-dimethoxyaniline hydrochloride (0·75 g.), at 210° gave a black mass which, chromatographed as above, gave the *indole* (from a yellow band), that crystallised from methanol as yellow plates, m. p. 133·5° (0·7 g.) (Found: C, 80·3; H, 5·9. $C_{32}H_{19}NO_3$ requires C, 80·2; H, 5·8%).

2,3-*Diphenylindole*-4,7-*quinone*.—(*a*) The above dimethoxyindole (1·0 g.) was demethylated as above with aluminium chloride (4·2 g.). After addition of acid, the product was extracted with ethyl acetate, and the dried organic layer was evaporated in nitrogen. The solid residue (0·6 g.) was immediately dissolved in acetone (70 ml.) and water (20 ml.) and oxidised with sodium dichromate (1·4 g.) in water (6 ml.) and concentrated sulphuric acid (2 ml.). After 30 min. the diluted solution was extracted with ether. Evaporation of the dried ether layer gave a dark red residue (0·48 g.) which was washed with a little benzene and then chromatographed on activated alumina in chloroform. Evaporation of the solvent which had eluted a red band left 2,3-diphenylindole-4,7-quinone which sublimed to form red needles above 190° and had m. p. 210° (decomp.).

(*b*) 4-Hydroxy-2,3-diphenylindole (0·3 g.) in acetone (15 ml.) was treated with potassium nitrosodisulphonate (0·7 g.) in water (30 ml.) and potassium dihydrogen phosphate (5 ml., M/6). The *quinone* recrystallised from aqueous alcohol as dark red needles which sublimed above 190° and had m. p. 216—218° (decomp.) (Found: C, 79·9; H, 4·5; N, 4·7. $C_{20}H_{13}NO_2$ requires C, 80·3; H, 4·3; N, 4·7%). The infrared spectra of the two samples were identical: $\nu_{max.}$ (in $CHCl_3$) 3400, 1660, 1645, 1595, 1435, 1280, 1105, 960, and a wide band 3300—2850 cm.$^{-1}$.

2,3-*Diphenylindole*-6,7-*quinone*.—(*a*) 6-Hydroxy-2,3-diphenylindole (made by demethylation of the 6-methoxy-compound) (0·5 g.) was oxidised with Fremy's salt (1·2 g.) as above. After ½ hr. the product was collected, washed, and dried. Chromatography in chloroform on activated alumina gave 2,3-diphenylindole-6,7-quinone, a red-brown solid which recrystallised from glacial acetic acid as dark red needles, not melting below 320° but decomposing slightly above 235° (Teuber and Schnee give m. p. 230°) (Found: C, 80·1; H, 4·5; N, 4·8. Calc. for $C_{20}H_{13}NO_2$: C, 80·3; H, 4·4; N, 4·7%), $\nu_{max.}$ (in $CHCl_3$) 3400, 1683, 1645, 1635, 1440, 1290, 982, 947, and a wide band 3300—2850 cm.$^{-1}$.

(*b*) 6-Hydroxydiphenylindole (purified chromatographically) (1·5 g.) was oxidised with Fremy's salt (3·6 g.). Chromatography as above gave a dark red band which was eluted rapidly, and evaporation of the solvent left the above 4,7-quinone (0·135 g.). Further elution slowly removed the 6,7-quinone.

4′,5′-*Diphenylpyrrolo*(2′,3′:1,2)*phenazine*.—(*a*) A mixture of the 6,7-quinone (1·0 g.) in acetic acid (100 ml.) and *o*-phenylenediamine (0·37 g.) in ethanol (8 ml.) was heated on a water-bath for 30 min. The solvents were partially removed *in vacuo* and dark orange crystals were collected and chromatographed in benzene on activated alumina. Elution of an orange band gave a solution which contained solid (0·8 g.), m. p. 120° (with frothing). This solid was melted and dissolved in boiling light petroleum (b. p. 60—80°) from which separated 4′,5′-*diphenylpyrrolo*(2′,3′:1,2)*phenazine*, orange needles, m. p. 143—145° (frothing above 150°) [Found (after drying at 150°): C, 84·0; H, 4·5. $C_{26}H_{17}N_3$ requires C, 84·1; H, 4·6%], $\nu_{max.}$ (in $CHCl_3$) 3600, 1625, 1600, 1470, 1440, 1350, 1325, 1290, 1133, 960, 905, and a wide band 3400—2850 with max. at 3375 and 3225 cm.$^{-1}$.

(*b*) The 6,7-quinone (0·5 g.) and *o*-phenylenediamine (0·37 g.) were heated in boiling pyridine (30 ml.) for 4 hr. The pyridine was distilled off and the brown residue was extracted with benzene which was then run on to activated alumina. The above phenazine (0·28 g.) was isolated by elution with benzene. The solid residue was recrystallised from xylene and gave yellow microcrystalline needles, m. p. 311—314° (0·1 g.) (Teuber and Schnee give m. p. 318—320°) (Found: C, 80·3; H, 4·9; N, 14·3. Calc. for $C_{32}H_{25}N_5$: C, 80·1; H, 5·25; N, 14·6. Calc. for $C_{32}H_{23}N_5$: C, 80·5; H, 4·8; N, 14·7%), unaltered by boiling acetic anhydride.

6-*Methoxy*-1-*methyl*-2,3-*diphenylindole*.—Dimethyl sulphate (5 ml.) was added during 1 hr. to a boiling solution of 6-hydroxydiphenylindole (2 g.) with powdered potassium hydroxide (3 g.) in acetone. After further boiling (1 hr.), water was added to precipitate the product which had m. p. 149° (from methanol) (Teuber and Schnee give m. p. 152°). Demethylation with aluminium chloride in benzene gave the corresponding 6-hydroxy-compound, m. p. 198—199° (Teuber and Schnee give m. p. 198—200°).

1-*Methyl*-2,3-*diphenylindole*-6,7-*quinone*.—This *quinone* was prepared from the above 6-hydroxy-*N*-methyl-compound (0·8 g.) with Fremy's salt (1·9 g.) and recrystallised from

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chloroform; it formed red needles which changed to plates at 210° and melted at 258—260° (Found: C, 80·3; H, 4·9; N, 4·6. $C_{21}H_{15}NO_2$ requires C, 80·5; H, 4·8; N, 4·5%), $\nu_{max.}$ (in $CHCl_3$) 1683, 1640, 1440, 1385, 1340, 1140, 1117, and 955 cm.$^{-1}$.

1′-Methyl-4′,5′-diphenylpyrrolo(2′,3′:1,2)phenazine was obtained from this *N*-methyl-6,7-quinone (0·4 g.) and *o*-phenylenediamine (0·14 g.) as above. It crystallised when the solvent was partially evaporated and recrystallisation from benzene gave yellow needles, m. p. 257—258° (0·24 g.) (Found: C, 83·8; H, 5·1. $C_{27}H_{19}N_3$ requires C, 84·1; H, 4·9%), $\nu_{max.}$ (in $CHCl_3$) 1605, 1555, 1465, 1427, 1355, 1335, 1143, 1120, 1090, and 890 cm.$^{-1}$.

The same compound (mixed m. p.) was obtained by methylating 4′,5′-diphenylpyrrolo-(2′,3′:1,2)phenazine with an excess of dimethyl sulphate and powdered potassium hydroxide in boiling acetone.

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682. *Free-radical Substitution in Aliphatic Compounds. Part III.*[1] *Halogenation of the 2-Halogenobutanes.*

By P. S. FREDRICKS and J. M. TEDDER.

The 2-halogenobutanes have been fluorinated, chlorinated, and brominated in the gas phase. The hydrogen atom most readily replaced by chlorine or bromine is that situated on the same carbon atom as the substituent halogen. Substitution of the hydrogen atoms attached to the adjacent carbon atoms is retarded for all halogenations. These results are in excellent accord with predictions based on previous study of the n-butyl halides.[1] Both the expected 2,3-dihalogenobutanes are formed in the chlorination and fluorination of these compounds, but the amounts of the two stereoisomers are not equal. A possible explanation of this observation is given.

THE halogenation of the secondary alkyl halides has received less study than the analogous reaction with the primary compounds. Two chlorinations of secondary alkyl chlorides [2,3] and the bromination of some secondary alkyl chlorides and bromides [4] comprise all the work that has been reported. The present study is a direct continuation of previous work [5,1] and has proved valuable in confirming ideas put forward on the basis of earlier results.

EXPERIMENTAL

As previously, the greatest problem was the correct identification of the products separated by gas chromatography.[1] The situation was more complicated in that there were now five dihalogenobutanes compared with the four obtained from the halogenation of the n-butyl halides. The principal method of identification was still the individual addition of the known dihalides to the reaction mixture. However, all such identifications were confirmed by elution of the material of each separate peak on the chromatogram and obtaining the infrared spectrum of the material causing each individual peak which was then compared with the infrared spectrum of the authentic material. Infrared spectra were also used to determine the relative proportions of two components which could not be completely resolved by chromatography. Spectra were obtained of the two authentic components and of synthetic mixtures of them, as well as of the unresolved mixture from the chromatogram. From these spectra the relative concentrations of the two components could readily be calculated. In two cases where the authentic compounds could not be synthesised the materials corresponding to the peaks were eluted from the chromatography column and their nuclear magnetic resonance spectra examined.

[1] Part II, Fredricks and Tedder, *J.*, 1960, 144.
[2] Tischenko and Churbakov, *Z. obshchei Khim.*, 1937, **7**, 663.
[3] Rust and Vaughan, *J. Org. Chem.*, 1941, **6**, 479.
[4] Kharasch, Zimmt, and Nudenberg, *J. Org. Chem.*, 1955, **20**, 1430.
[5] Anson, Fredricks, and Tedder, *J.*, 1959, 918.

Preparation of Authentic Dihalides for Identification.—The preparation of 1,2-dichlorobutane, 1,3-dichlorobutane, and 1,3-difluorobutane has been described previously.[1] 2,2-Dichlorobutane [6] was prepared from ethyl methyl ketone by treatment with phosphorus pentachloride. Racemic and *meso*-2,3-dichlorobutane [7] were prepared by the addition of chlorine to but-2-ene.[8] 2-Chloro-2-fluorobutane [9] and 2,2-difluorobutane [6] were prepared from 2,2-dichlorobutane by treatment with antimony trifluoride containing 5% of bromine. The 2-chloro-3-fluorobutanes and 2,3-difluorobutanes were prepared from 2,3-dichlorobutane by treatment with mercuric oxide and hydrogen fluoride. The products were characterised by their infrared spectra and retention times. It was assumed that the *erythro*-derivatives were eluted first by analogy with the 2,3-dichlorobutanes. 1-Chloro-3-fluorobutane was prepared from 1,3-dichlorobutane by the same method; none of the isomeric 3-chloro-1-fluorobutane was formed.

Apparatus and Experimental Techniques.—These were identical with those described previously.[1,5]

Chlorination of 2-Chlorobutane.—Results for an initial mixture of 2-chlorobutane (11 parts), chlorine (1 part), and nitrogen (360 parts) were:

Temp.	No. of runs	CH_3—	—CHCl—	—CH_2— (*meso*)	—CH_2— (±)	—CH_3
35°	7	4·1 ± 0·7	26·3 ± 0·7	51·0 ± 0·5 (36·4 ± 1·1)	(14·6 ± 0·6)	18·6 ± 0·9
78	6	4·3 ± 0·9	26·2 ± 1·1	49·8 ± 1·3 (35·0 ± 1·2)	(14·8 ± 0·6)	19·7 ± 0·8

Identification of products. There were five peaks on the chromatogram and these were identified by the individual addition of the authentic dihalides to the reaction products.

Chlorination of 2-Fluorobutane. Products from an initial mixture of 2-fluorobutane (10 parts), chlorine (1 part), and nitrogen (400 parts) were:

Temp.	No. of runs	2-Cl,2-FC_4H_8	(±)-2-Cl,3-FC_4H_8 (*erythro*)	(*threo*)	1-Cl,2-F- + 1-Cl,3-FC_4H_8
35°	10	35·6 ± 2·1	41·6 ± 1·3 (24·7 ± 0·9)	(16·9 ± 0·9)	22·8 ± 1·5
78	11	33·0 ± 1·7	40·6 ± 2·2 (24·2 ± 1·8)	(16·4 ± 1·3)	26·4 ± 3·1

Identification of products. There were only four peaks on the chromatogram. The first three materials eluted were identified as 2-chloro-2-fluorobutane, and the two racemic 2-chloro-3-fluorobutanes by addition of authentic material to the products. This was checked by comparing the infrared spectra of the components of the product with those of authentic materials. Because the synthesis of the two " authentic " 2-chloro-3-fluorobutanes was not completely unambiguous the materials corresponding to the second and third peaks from the reaction mixture were eluted and their nuclear magnetic resonance spectra examined. The proton spectra were observed for both compounds. The majority of protons in the molecules had similar chemical shifts, *i.e.*, there were two methyl groups. Besides the intense group of lines due to the methyl groups there were two less intense groups due to the 2- and 3-hydrogen atoms. These facts together with the fine details of the spectra indicated that the two peaks on the chromatogram were in fact the two racemates of 2-chloro-3-fluorobutane. The final peak on the chromatogram had a retention time corresponding to that due to 1-chloro-2-fluoro- plus 1-chloro-3-fluoro-butane obtained from the fluorination of 1-chlorobutane.[1] Judged from the amount of 1,2-dichlorobutane produced in the chlorination of 2-chlorobutane (see above) it would be expected that the amount of 1-chloro-2-fluorobutane produced in the present experiment would be very small. This was confirmed by examination of infrared spectra; the spectrum corresponding to the peak due to 1-chloro-2-fluoro- plus 1-chloro-3-fluoro-butane from the present experiment was compared with that of authentic 1-chloro-3-fluorobutane to which it was very similar. It was also compared with the spectrum of the material of the

[6] Henne, Renoll, and Leicester, *J. Amer. Chem. Soc.*, 1934, **61**, 938.
[7] Lucas and Gould, *J. Amer. Chem. Soc.*, 1941, **63**, 2541.
[8] Davis, *J. Amer. Chem. Soc.*, 1928, **50**, 2779.
[9] Henne and Hinkamp, *J. Amer. Chem. Soc.*, 1945, **67**, 1194.

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analogous peak from the fluorination of n-butyl chloride which showed several extra absorption bands due to the 1-chloro-2-fluorobutane.

Fluorination of 2-Fluorobutane.—A mixture of 2-fluorobutane (10 parts), fluorine (2 parts), and nitrogen (400 parts) gave the following products:

Temp.	No. of runs	*meso*-2,3-$F_2C_4H_8$	(±)-2,3- + 1,3-$F_2C_4H_8$	1,2-$F_2C_4H_8$
21°	7	19·2 ± 1·9	56·9 ± 1·2	23·9 ± 0·9

Identification of products. There were only three peaks on the chromatogram. Addition of authentic 2,2-difluorobutane showed that this isomer would be eluted with the unchanged butyl fluoride. The first of the three peaks was shown to be due to 2,3-difluorobutane by addition of authentic material. It was assumed to be the *meso*-isomer by analogy with the dichlorides. The final peak was identified as due to 1,2-difluorobutane on the basis of retention time and infrared spectrum compared with those of 1,2-difluorobutane from the fluorination of n-butyl fluoride. The middle peak was shown to contain both 2,3-difluorobutane [assumed to be (±)] and 1,3-difluorobutane by addition of authentic materials. The infrared spectrum of this mixture was compared with those of mixtures containing the authentic 1,3-difluorobutane and (±)-2,3-difluorobutane of known concentration. By using an absorption band at 848 $cm.^{-1}$ for 1,3-difluorobutane where there was no absorption from (±)-2,3-difluorobutane, and bands at 1178 $cm.^{-1}$ and 933 $cm.^{-1}$ for (±)-2,3-difluorobutane where there was only moderate absorption from 1,3-difluorobutane, it was possible to calculate the proportions of the two isomers in the product. From four synthetic mixtures the ratio of [1,3-$C_4H_8F_2$]/[(±)-2,3-$C_4H_8F_2$] was estimated to be 3·58 : 1.

Fluorination of 2-Chlorobutane.—The mixture, 2-chlorobutane (10 parts), fluorine (5 parts), and nitrogen (400 parts) gave the following products:

Temp.	No. of runs	(±)-*erythro*-2-Cl, 3-FC_4H_8	(±)-*threo*-2-Cl, 3-F- + 2-Cl, 1-F-C_4H_8	3-Cl, 1-FC_4H_8
21°	4	17·0 ± 0·9	16·3 ± 0·2	66·6 ± 0·8

Identification of products. There were only three chlorofluorobutane peaks on the chromatogram. The first of these was not completely resolved from the unchanged 2-chlorobutan- when the normal proportions of the reactants were used. By increasing the extent of fluorine ation it was possible to inject less material into the column and so resolve the first peak previously obtained. It was found to be a (±)-2-chloro-3-fluorobutane by the addition of authentic material. The last peak to be eluted was similarly shown to be due to 3-chloro-1-fluorobutane. The centre peak was shown to contain the other (±)-2-chloro-3-fluorobutane, by addition of authentic material, and 2-chloro-1-fluorobutane, by comparison with the chromatogram of chlorinated 1-fluorobutane. All these identifications were confirmed by examination of the infrared spectra of the materials of the individual peaks. The proportions of the second racemic 2-chloro-3-fluorobutane and 2-chloro-1-fluorobutane corresponding to the centre peak were estimated from the infrared spectrum by using synthetic mixtures made up from the authentic 2-chloro-3-fluorobutane racemate and 2-chloro-1-fluorobutane from the chlorination of n-butyl fluoride. The spectrum of 2-chloro-1-fluorobutane had a strong band at 845 $cm.^{-1}$ in which region racemic 2-chloro-3-fluorobutane did not absorb; similarly 2-chloro-3-fluorobutane had a strong band at 895 $cm.^{-1}$ in which region 2-chloro-1-fluorobutane was completely transparent. The ratio of the isomers so obtained was [$CH_3F{\cdot}CHCl{\cdot}C_2H_5$]/[$CH_3{\cdot}CHCl{\cdot}CHF{\cdot}CH_3$] = 0·9 : 1. The infrared spectra and the chromatogram showed that the more extensive fluorination had resulted in the formation of small amounts of trihalogenobutanes and the results of these experiments are likely therefore to be less accurate than the others.

Bromination of 2-Fluorobutane.—Reaction of 2-fluorobutane (10 parts), bromine (1 part), and nitrogen (400 parts) was carried out at 146°. There was only one large dihalide peak on the chromatogram, although two small subsequent peaks were just discernible. The material of the main peak was examined by nuclear magnetic resonance spectroscopy; both proton and fluorine-19 spectra were observed and they clearly showed that the product was 2-bromo-2-fluorobutane. By injecting large samples into the chromatograph it was possible to make the very small second and third peaks large enough for their relative areas to be estimated. It seems probable that these two peaks were the two racemic 2-bromo-3-fluorobutanes in proportions 64·3% of *erythro* and 35·7% of *threo*. The two isomers represented less than 8% of the detected bromofluorobutane.

Bromination of 2-Bromobutane.—Reaction of 2-bromobutane (10 parts), bromine (1 part), and nitrogen (400 parts) was carried out at 146° and, unlike the bromination of n-butyl bromide, proceeded smoothly. There was only one large product peak on the chromatogram and this was shown by nuclear magnetic resonance spectroscopy to be due to 2,2-dibromobutane. There were two very small, badly defined peaks subsequent to the 2,2-dibromobutane peak which may have been due to the two 2,3-dibromobutanes but the concentrations were too small to permit any further investigation.

Bromination of 2-Chlorobutane. Reaction of 2-chlorobutane (11 parts), bromine (1 part), and nitrogen (400 parts) was carried out at 146°. The chromatogram had only one large peak in addition to that due to unchanged 2-chlorobutane. By analogy with the preceding two experiments this single product was assumed to be 2-bromo-2-chlorobutane.

Competitive Chlorination of 1-Chloro- and 2-chloro-butane.—A mixture (10 parts) of 1- and 2-chlorobutane was placed in a trap surrounded by a constant-temperature bath at 0°, and a vapour mixture was entrained into the reactor by bubbling nitrogen (in all 400 parts) through the liquid. The relative concentrations of the two components in the vapour entering the reactor was determined by diverting the gas stream through a second trap in which the butyl halides were recondensed. By this means, samples of the reactants could be obtained at intervals while the chlorination (by 1 part of chlorine) was in progress. The ratio of the two butyl chlorides varied only very slightly during the chlorination provided the quantity of liquid mixture in the initial trap was fairly large. The chlorinated products were collected and analysed as before:

Temp.	No. of runs	Reactants $2\text{-ClC}_4\text{H}_9 : 1\text{-ClC}_4\text{H}_9$	Products % ($C_4H_8Cl_2$) 1,3-	1,4-
35°	6	0·99 ± 0·03	77·8 ± 1·9	22·2 ± 1·9
78	7	0·95 ± 0·09	76·3 ± 2·1	23·7 ± 2·1

Discussion

It is important that the present results should be related to the previous work on the halogenation of butane and the n-butyl halides. It seems reasonable to assume that the 2-position of 2-halogenobutanes will be affected in a similar fashion to the 1-position in the 1-halogenobutanes. The chlorination results in Table 1 have been calculated on this

Table 1. *The chlorination of 2-halogenobutanes;* RS_p^x.

Temp.	X	CH_3———CHX	———CH_2———CH_3	
35°	H	1	3·9$_5$	3·9$_5$ 1
78	H	1	3·6	3·6 1
35	Cl	0·2	3·2	3·1 0·8
78	Cl	0·2	3·0	2·9 0·8
35	F	<0·1	3·6	2·1 0·7
78	F	<0·1	3·2	2·0 0·7

assumption, the validity of which was checked by the competitive chlorination of 1-chlorobutane and 2-chlorobutane. The relative proportions of 1,3- and 1,4-dichlorobutane formed as a result of the chlorination of 1-chlorobutane were already known so that the rate of chlorination of carbon atom 4 in 2-chlorobutane could be compared with rate of chlorination of carbon atom 4 in 1-chlorobutane by competitive chlorination. The results gave RS_p^4 for 2-chlorobutane as 0·76 ± 0·4 (calc. 0·8; cf. Table 1) at 35°, and as 0·82 ± 0·38 (calc. 0·8) at 78°. The striking feature of the above results is that the most reactive site in 2-halogenobutanes is the one bearing the substituent halogen. This is in agreement with the results of Rust and Vaughan [3] and emphasises how misleading was the previously accepted generalisation that the substituent halogen directs attack away from itself.[10] Comparison of the present results with the previous work on n-butyl halides confirms the importance of hyperconjugation in determining the reactivity of a particular hydrogen atom.[11] For instance, the hydrogen atoms on carbon atom 1 in 2-chlorobutane, carbon atom 2 in 1-chlorobutane, and carbon atom 3 in 2-chlorobutane are all the same distance

[10] Brown and Ash, *J. Amer. Chem. Soc.*, 1955, **77**, 4019.
[11] Fredricks and Tedder, *Chem. and Ind.*, 1959, 490.

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from the substituent chlorine, yet their reactivities *relative to the corresponding sites in unsubstituted butane* are approximately 0·2, 0·6, and 0·8, respectively. The extent of deactivation due to the inductive effect of the substituent halogen must be the same for each position, but the change in hyperconjugation at each position due to the substituent is very different.

There is no simple method for relating the results of the fluorination of the 2-halogenobutanes with those of previous work. However, the noticeable feature of Table 2 is the

TABLE 2. *The fluorination (%) of the 2-halogenobutanes.*

Temp.	X	CH_3———CHX———CH_2———CH_3			
20°	F	23·9	—	31·9	44·2
20	Cl	7·9	—	25·5	66·6

small proportions of 2-chloro-1-fluoro- and 2-chloro-3-fluoro-butane obtained by the fluorination of 2-chlorobutane. There is little doubt that this is the " vicinal effect " previously observed in the chlorination of 1-bromobutane and in 1-chlorobutane at high temperatures.[3,1] These results indicate that the intermediate chlorobutyl radical loses chlorine even at room temperature. This effect is probably masked in the chlorinations by the subsequent addition of chlorine to the butene so formed. Another explanation of the large vicinal effect in fluorination would be that the chlorobutyl radicals are relatively hot when formed in fluorination, but this seems less likely, for although the hydrogen abstraction step is very exothermic, most of this heat will be found in the hydrogen fluoride molecule rather than in the new radical.[12]

The almost exclusive attack at the 2-position by bromine atoms in the 2-halogenobutanes was expected. The bromination of n-butyl fluoride and chloride had shown that the substituent halogen accelerated substitution at the carbon atom to which it is attached by a factor of greater than ten, while at the same time reducing the reactivity of the adjacent positions by a factor of two or more.

The halogenation of the 2-halogenobutanes as expected yielded two 2,3-dihalogenobutanes. It is of considerable interest that the two 2,3-isomers are not formed in equal amounts (cf. Table 3; it has been assumed that the first 2,3-isomer to be eluted is invariably

TABLE 3. *The proportions of* erythro- *and* threo-2,3-*isomers formed during the halogenation of the 2-halogenobutanes.*

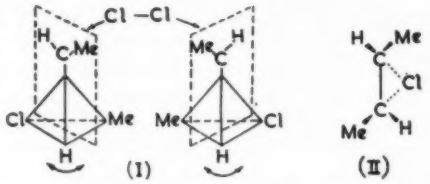
	Temp.	*erythro* (%)	*threo* (%)
(*a*) Chlorination of 2-chlorobutane:	35°	71·4	28·6
	75	70·3	29·7
(*b*) Chlorination of 2-fluorobutane:	35	59·4	40·6
	75	59·6	40·4
(*c*) Fluorination of 2-chlorobutane:	21	66·6	33·4
(*d*) Fluorination of 2-fluorobutane:	21	60·2	39·8

the *erythro*-compound). On the chromatogram from the bromination of 2-fluorobutane there were two small peaks eluted after the 2-bromo-2-fluorobutane, which was the major product. It seems probable that these small peaks were the 2-bromo-3-fluorobutanes. If this is so and the *erythro*-compound was eluted first, then the proportions of the two isomers were 64·3% *erythro* and 35·7% of *threo*.

These results clearly imply that the reaction between the intermediate 2-halogeno-1-methylpropyl radicals ($CH_3 \cdot CHX \cdot \dot{C}H \cdot CH_3$) and the halogen molecule is stereospecific. A possible explanation is that the two such radicals have preferred conformations both of which favour substitution from one direction. If it is assumed that the bonds about the tervalent carbon atom approximate to sp^2 and are nearly planar, then the other three bonds on the tetrahedral carbon can rotate relatively to this plane. However they can be expected to have a preferred conformation in which the methyl group of the tervalent carbon atom

[12] Smith, *J. Chem. Phys.*, 1959, **31**, 1352; Polanyi, *ibid.*, p. 1338.

will be closely above the hydrogen atom of the tetrahedral carbon, slightly to either side (see the Figure). The incoming halogen molecule must approach approximately



perpendicularly to the free-radical plane and this approach will be easier on the side away from the substituent halogen atom so that in both cases it will yield the *erythro*-compound. Table 3 shows that the size of the substituent halogen has a greater effect on the proportion of the two stereoisomers formed, than the reactivity of the attacking atom. This would agree with the suggested mechanism. An alternative explanation involving the bridged structure (II) which would occur most readily with the methyl groups in a "*trans*"-position, seems unlikely as no evidence for migration of halogen atoms has been observed during any of these halogenations.

Stereospecificity in free-radical reactions of the type reported here was previously observed by Kooyman and Vegter.[13] They halogenated norbornane (bicyclo[2,2,1]-heptane) in the gas and liquid phases and found that the 2 position was the most reactive. Of the two possible isomers the *exo*-compound predominated. The explanation offered by Kooyman and Vegter was essentially identical with that offered in the present paper.

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UNIVERSITY OF SHEFFIELD. [*Received, September 28th*, 1960.]

[13] Kooyman and Vegter, *Tetrahedron*, 1958, **4**, 382.

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683. *Investigations on the Synthesis of 2-Acetylcyclohex-2-enone. Part II.*[1] *Some Related Experiments, and the Constitution of the Dimeric Product,* $C_{16}H_{20}O_4$.

By C. W. T. HUSSEY and A. R. PINDER.

Dehydrochlorination of 2-acetyl-2-chlorocycloheptanone yields an enolic product formulated as (XIII). The properties of this product, and that derived similarly from 2-acetyl-2-chlorocyclohexanone,[1] and the comparative stability of 2-acetyl-2-chloro-4,4-dimethylcyclohexanone towards base, suggest that 2-acylcycloalk-2-enones are unstable, and stabilise themselves by enolisation.

The structure (XXII), derived from tricyclo[6,2,2,$0^{2,7}$]dodecane, is advanced for the dimeric product $C_{16}H_{20}O_4$ described in Part I.[1]

EXPERIMENTS described in Part I [1] of this series were concerned with the dehydrochlorination of 2-acetyl-2-chlorocyclohexanone (I; R = H), which led to an enolic compound formulated, not as the expected (II; R = H), but as (III), existing chiefly as its enolic

[1] Part I, McEntee and Pinder, *J.*, 1957, 4419.

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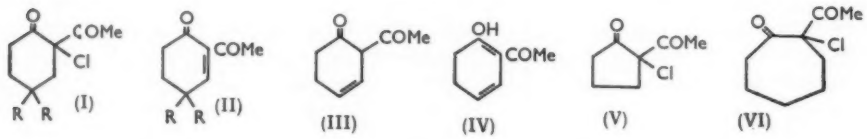
form (IV). A dimeric product $C_{16}H_{20}O_4$, believed to be the dimer of (II; R = H), was formed simultaneously.

Because of the restricted manner in which dehydrochlorination may occur, it was of interest to study the behaviour of 2-acetyl-2-chloro-4,4-dimethylcyclohexanone (I; R = Me) on treatment with base. The chloro-ketone was obtained from 4,4-dimethylcyclohexanone by acetylation followed by treatment with sulphuryl chloride. It proved to be remarkably stable to the action of collidine. Even after prolonged treatment more than half was recovered, and the amount of collidine hydrochloride formed was less than half that expected; the main product was tar. A trace of alkali-soluble material was obtained when the reaction was conducted on a large scale, but this, on spectral and chemical



evidence, was 2-acetyl-4,4-dimethylcyclohexanone. The reductive elimination of halogen atoms during treatment with collidine has been reported in the steroid field.[2] This unsuccessful attempt to force the dehydrochlorination (I ⟶ II; R = Me) suggests that in a cycloalkenone system a double bond in the 2,3-position in cross-conjugation with two carbonyl groups is unstable. A similar instability has been noted with certain acyclic model compounds.[1]

Similar dehydrochlorinations of 2-acetyl-2-chlorocyclopentanone (V) and 2-acetyl-2-chlorocycloheptanone (VI) have been examined. Neither chloro-compound showed enolic properties; the chlorine atoms are therefore correctly placed at position 2. On treatment with collidine and other basic reagents the former yielded tar accompanied by unchanged chloro-ketone; the latter afforded approximately one mol. of collidine hydrochloride and a volatile product $C_9H_{12}O_2$, which on catalytic hydrogenation gave 2-acetylcycloheptanone, with uptake of one mol. of hydrogen. This product is therefore an acetylcycloheptenone, and formulæ (VII)—(XI) have to be considered.

The product $C_9H_{12}O_2$ is enolic in its behaviour, being readily soluble in aqueous alkali, giving a deep purple ferric test, forming a copper complex, and having a typical conjugate chelate infrared absorption curve. On careful oxidation with permanganate it yielded only glutaric acid. This observation eliminates structures (IX) and (X), and their respective enolic forms (XIV) and (XV). We feel also that the structure (XI), with its enol (XVI), can be eliminated by analogy with the behaviour of 2-acetyl-2-chlorocyclohexanone (I; R = H), which we showed gave a product different from 2-acetylcyclohex-5-enone.[1] Further, it is unlikely that a double bond would appear in the 6,7-position as a result of the elimination of a chlorine atom at position 2.

Of the remaining structures, (VIII) would enolise to (XIII). Theoretically, (VII) could enolise to (XII), *via* the reactive methylene group at position 7, but such an enolisation usually requires additional activation of the hydrogen atoms concerned. Further, the enol (XII) cannot be stabilised by resonance between zwitterionic forms.[3] Enolisation might, however, involve the allylic methylene group at position 4, and this would lead to (XIII), so that (VII) and (VIII) would have a common enolic form. The most satisfactory explanation of the properties of the compound $C_9H_{12}O_2$ seems to be that it is 2-acetylcyclohept-2-enone (VII), but that owing to the instability of the doubly conjugated 2,3-double bond, as shown by the behaviour of the analogue (I; R = Me) on dehydrochlorination, the compound stabilises itself by enolisation, its structure being therefore (XIII).

[1] Cf. Schwenk and Whitman, *J. Amer. Chem. Soc.*, 1937, **59**, 949; Jacobsen, *ibid.*, 1940, **62**, 1620.
[3] Cf. Smith, *J.*, 1953, 803.

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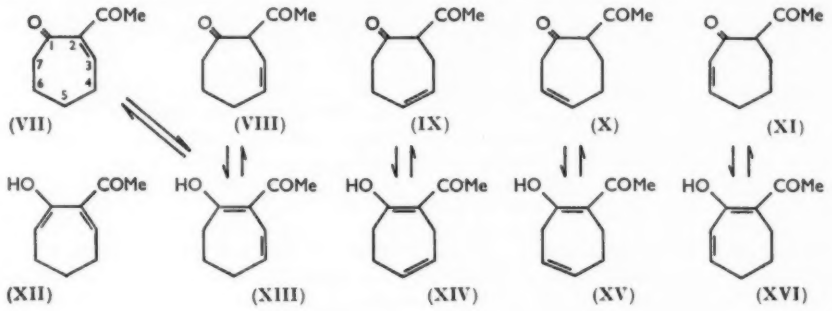
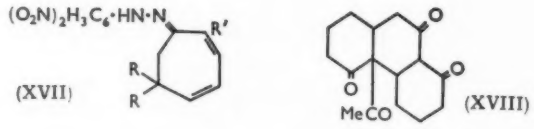
The corresponding compound in the cyclohexane series [1] we regard as (IV), derived from (II; R = H) by a similar stabilisation.

Alkaline hydrolysis of the compound $C_9H_{12}O_2$ gave a neutral product, as well as acetic acid and a syrupy unsaturated keto-acid which could not be purified. The keto-acid



resulted from ring scission; analogous hydrolyses of 2-acylcyclopentanones and 2-acylcyclohexanones yield keto-acids.[4] The neutral hydrolysis product was treated with 2,4-dinitrophenylhydrazine and the resulting derivative subjected to chromatography, whereby



it was separated into cycloheptanone 2,4-dinitrophenylhydrazone and a deep red derivative, m. p. 201—202°. The latter showed a depression in m. p. on admixture with cyclohept-2-enone 2,4-dinitrophenylhydrazone, m. p. 122°, $\lambda_{max.}$ 377 mμ, prepared by the dehydrobromination of 2-bromocycloheptanone.[5] The analysis and ultraviolet absorption [max. at 385 mμ; ε = 29,600 (in chloroform); compare eucarvone 2,4-dinitrophenylhydrazone (XVII; R = R' = Me), $\lambda_{max.}$ 388 mμ, ε = 27,450 (in chloroform) [6]] suggest that it is cyclohepta-2,4-dienone 2,4-dinitrophenylhydrazone (XVII; R = R' = H). This functional derivative of cyclohepta-2,4-dienone has been described by Dewar and Pettit,[7] who have recorded its m. p. as 149—150°. We feel that the difference here may be accounted for either by dimorphism or, more probably, by *cis–trans*-isomerism. Cyclohepta-2,4-dienone and cycloheptanone have presumably arisen by disproportionation of cyclohept-2-enone, the true hydrolysis product.

Some preliminary studies on the structure of the dimeric product $C_{16}H_{20}O_4$ were described in Part I [1]. It was assumed that the product resulted from the dimerisation of 2-acetylcyclohex-2-enone (II; R = H), but the structure (XVIII), analogous to that of the dimer of 1-acetylcyclohexene,[8] was rejected because the dimer contains no non-enolisable carbonyl group, and two *C*-methyl groups. The dimerisation is therefore apparently

[4] Hauser, Swamer, and Ringler, *J. Amer. Chem. Soc.*, 1948, **70**, 4023; Manyik, Frostick, Sanderson, and Hauser, *ibid.*, 1953, **75**, 5030.
[5] Braude and Evans, *J.*, 1954, 607.
[6] Campbell, Islam, and Raphael, *J.*, 1956, 4096.
[7] Dewar and Pettit, *J.*, 1956, 2021.
[8] Jones and Koch, *J.*, 1942, 393.

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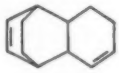
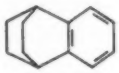
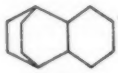
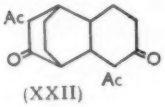
of a cyclohex-2-enone rather than of an acetylcyclohexene. Examples of the base-catalysed dimerisation of cyclohex-2-enones have been described frequently in the literature; they invariably involve Michael addition reactions,[9] and small rings are not usually formed under these conditions.[10]

The dimer yielded on hydrolysis acetic acid, a syrupy keto-acid which could not be characterised, and a diketone $C_{12}H_{16}O_2$, containing no *C*-methyl groups. This diketone afforded a tripiperonylidene derivative, the formation of which proved the presence of


(XIX)


(XX)

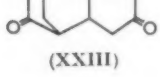

(XXI)

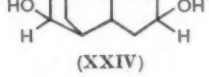


(XXII)

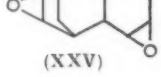
three reactive methylene groups. Wolff–Kishner reduction of the diketone yielded a saturated hydrocarbon $C_{12}H_{20}$, which must be tricyclic. Reduction of the diketone with lithium aluminium hydride gave a diol $C_{12}H_{20}O_2$, which when heated with palladised carbon was dehydrated and dehydrogenated to a mixture of hydrocarbons with an odour strongly reminiscent of tetralin. On infrared evidence this product was a mixture containing a high proportion of an *ortho*-disubstituted benzenoid hydrocarbon, probably tetralin itself. A similar product resulted from dehydrogenation of the hydrocarbon $C_{12}H_{20}$.

The behaviour on dehydrogenation resembles that of the tricyclic hydrocarbon (XIX), the dimer of cyclohexa-1,3-diene,[11] and one of its dihydro-derivatives, which yield naphthalene [12] and 1,4-ethylene-1,2,3,4-tetrahydronaphthalene (XX).[13] It seemed likely


(XXIII)



(XXIV)


(XXV)

therefore that our $C_{12}H_{20}$ hydrocarbon was tricyclo[6,2,2,0 ^{2,7}]dodecane (XXI); this hydrocarbon was prepared by catalytic hydrogenation of the cyclohexadiene dimer (XIX).[14] It proved to be identical in b. p. and refractive index with the $C_{12}H_{20}$ hydrocarbon, and the two infrared absorption curves were superimposable. The carbon framework of the $C_{12}H_{20}$ hydrocarbon, the diol $C_{12}H_{20}O_2$, and the diketone $C_{12}H_{16}O_2$ is therefore established. If it is assumed that dimerisation of 2-acetylcyclohex-2-enone, by the mutual Michael addition of two molecules, is involved, the only possible structure for the dimer $C_{16}H_{20}O_4$ consistent with the established constitution for the $C_{12}H_{20}$ hydrocarbon is (XXII). The diketone and the diol are then formulated as (XXIII) and (XXIV) respectively.

An attempt was made to synthesise the diketone (XXIII) from the diene (XIX), which was converted by perbenzoic acid into the diepoxide (XXV). The latter, however, was not rearranged by treatment with lithium diethylamide in ether.[15]

[9] See, for example, Knoevenagel and Reinecke, *Ber.*, 1899, **32**, 418; Treibs, *Ber.*, 1930, **63**, 2738; *J. prakt. Chem.*, 1933, **138**, 299; Briggs, Harland, Ralph, and Simmonds, *J.*, 1953, 3788; Taylor, *Chem. and Ind.*, 1954, 252; Ayer and Taylor, *J.*, 1955, 2227; Büchi, Hansen, Knutson, and Koller, *J. Amer. Chem. Soc.*, 1958, **80**, 5517.

[10] Mustafa, *Chem. Rev.*, 1952, **51**, 1; de Mayo, *Adv. Org. Chem.*, 1960, **2**, 387.

[11] Alder and Stein, *Annalen*, 1932, **496**, 197.

[12] Hofmann, *Chem.-Ztg.*, 1933, **57**, 5.

[13] Kazanskii and Vol'fson, *J. Gen. Chem.* (*U.S.S.R.*), 1938, **8**, 1685.

[14] Alekseevskii, *J. Gen. Chem.* (*U.S.S.R.*), 1939, **9**, 1586.

[15] Cope, Trumbull, and Trumbull, *J. Amer. Chem. Soc.*, 1958, **80**, 2844.

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Experimental

2-Acetyl-2-chlorocyclopentanone (V).—2-Acetylcyclopentanone [16] (18·7 g., 0·15 mol.) in carbon tetrachloride (84 c.c.) was stirred at room temperature during the gradual (1 hr.) addition of sulphuryl chloride (22·0 g., 0·16 mol.) in carbon tetrachloride (30 c.c.). After being stirred for a further 12 hr. the solution was shaken with water and aqueous sodium hydrogen carbonate and dried. The solvent was removed under reduced pressure through a short Vigreux column, and the residual *2-acetyl-2-chlorocyclopentanone* distilled; it had b. p. 92—94°/13 mm. (17·2 g.) (Found: C, 51·6; H, 5·85; Cl, 22·6. $C_7H_9ClO_2$ requires C, 52·3; H, 5·6; Cl, 22·1%), and, as liquid film, carbonyl bands at 1714 and 1754, and a C–Cl band at 766 cm.$^{-1}$. The compound gave no colour with alcoholic ferric chloride.

Attempts to dehydrochlorinate the product by heating it with collidine, pyridine, methanolic sodium methoxide, or methanolic potassium acetate afforded tar and unchanged chloro-ketone.

2-Acetyl-2-chlorocycloheptanone (VI).—A similar chlorination of 2-acetylcycloheptanone [17] (20 g.) in carbon tetrachloride (90 c.c.) with sulphuryl chloride (19·3 g.) in carbon tetrachloride (35 c.c.) yielded *2-acetyl-2-chlorocycloheptanone* (21·6 g.), b. p. 112—114°/10 mm. (Found: C, 56·7; H, 6·9. $C_9H_{13}ClO_2$ requires C, 57·3; H, 6·9%), $\nu_{max.}$ (liquid film) at 1707 and 1723 (C=O), and 767 cm.$^{-1}$ (C–Cl). The product gave no colour with alcoholic ferric chloride. The *2,4-dinitrophenylhydrazone*, prepared in cold, alcoholic solution, crystallised from ethanol in golden-yellow needles, m. p. 165° (decomp.) (Found: C, 49·0; H, 4·65. $C_{15}H_{17}ClN_4O_5$ requires C, 48·8; H, 4·65%).

2-Acetylcyclohepta-1,3-dien-1-ol (XIII).—A mixture of 2-acetyl-2-chlorocycloheptanone (5 g.) and collidine (15 c.c.) was heated at 180° for 2½ hr. The cooled mixture was diluted with ether, and the collidine hydrochloride removed. The ethereal filtrate was shaken in turn with dilute hydrochloric acid, dilute sodium hydroxide, and water, and dried. Evaporation of the ether yielded only tar. The alkaline extract was cooled, acidified with 5N-hydrochloric acid, and extracted with ether. Evaporation of the dried extract afforded *2-acetylcyclohepta-1,3-dien-1-ol*, b. p. 97—98°/8 mm., 102°/10 mm. (1·8 g.) (Found: C, 71·8; H, 8·4. $C_9H_{12}O_2$ requires C, 71·1; H, 7·9%). Infrared absorption (liquid film) showed a typical conjugate chelate spectrum, with bands at 3020 (OH), 1590 (C=O), and 701 cm.$^{-1}$ (*cis*-CH=CH). The compound was soluble in aqueous sodium hydroxide, gave a deep purple ferric test, and formed a *copper complex*, which separated from benzene–light petroleum (b. p. 60—80°) in green needles, m. p. 180—181° (Found: C, 59·2; H, 6·4. $C_{18}H_{22}CuO_4$ requires C, 59·1; H, 6·0%). On catalytic hydrogenation in ethanol at room temperature and pressure in the presence of 5% palladised charcoal, the compound absorbed one mol. of hydrogen with the formation of 2-acetylcycloheptanone, identified as its *copper complex*, grey needles [from benzene–light petroleum (b. p. 60—80°)], m. p. and mixed m. p. 210—211° (Found: C, 58·65; H, 6·8. $C_{18}H_{24}CuO_4$ requires C, 58·3; H, 7·0%).

Oxidation of 2-Acetylcyclohepta-1,3-dien-1-ol.—A solution of the foregoing enol (2·5 g.) in dry, permanganate-stable acetone (75 c.c.) was stirred at 0—5° whilst finely powdered potassium permanganate was added gradually, until a permanent pink colour was observed. After a further hour's stirring the solution was filtered and the residue dried at room temperature. It was mixed with water (150 c.c.) and the mixture filtered from manganese dioxide. Excess of permanganate was destroyed by the addition of a little solid sodium hydrogen sulphite, and the solution acidified with 5N-hydrochloric acid and subjected to continuous ether-extraction overnight. Evaporation of the dried extract yielded glutaric acid (0·7 g.), m. p. and mixed m. p. 97—98°.

Action of Aqueous Alkali on 2-Acetylcyclohepta-1,3-dien-1-ol.—The enol (2·0 g.) was refluxed for 2 hr. with 5% aqueous sodium hydroxide (15 c.c.). The cooled solution was extracted several times with ether, and the extracts were dried and evaporated through a short Vigreux column. The residual oil distilled at 56—57°/9 mm. (0·24 g.); it was mixed with alcoholic 2,4-dinitrophenylhydrazine sulphate and the orange-red precipitate collected and purified by chromatography in chloroform solution on bentonite–kieselguhr. Elution with chloroform gave, after evaporation, cycloheptanone 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 147°. Further elution with chloroform–ethanol afforded, after evaporation, a *product* which

[16] *Org. Synth.*, Coll. Vol. II, 1943, p. 531.
[17] Buchta and Kranz, *Angew. Chem.*, 1955, **67**, 77.

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crystallised from ethyl acetate in deep red needles, m. p. 201—202° (Found: C, 54·3; H, 4·6; N, 19·4. $C_{13}H_{12}N_4O_4$ requires C, 54·2; H, 4·2; N, 19·4%), $\lambda_{max.}$ (in chloroform) 385 mμ (ε 29,600). Dewar and Pettit [7] give cyclohepta-2,4-dienone 2,4-dinitrophenylhydrazone, m. p. 149—150°.

Acidification of the original alkaline solution gave acetic acid (*S*-benzylthiouronium salt, m. p. and mixed m. p. 136°), and a gummy acid, isolated with ether. The latter was unsaturated and ketonic, but could not be converted into a crystalline derivative.

2-Acetyl-4,4-dimethylcyclohexanone.—4,4-Dimethylcyclohexanone was synthesised from *p*-cresol, through 4-dichloromethyl-4-methylcyclohexa-2,5-dienone [18] and 4,4-dimethylcyclohexanol.[19,20] The *2,4-dinitrophenylhydrazone* crystallised from ethanol in orange-yellow needles, m. p. 148—149° (Found: C, 54·4; H, 6·0; N, 18·7. $C_{14}H_{18}N_4O_4$ requires C, 54·9; H, 5·9; N, 18·3%). The ketone (10·6 g.) was mixed with acetic anhydride (17·1 g.), and the solution was saturated with boron trifluoride at 0°. Working up in the usual manner [21] gave *2-acetyl-4,4-dimethylcyclohexanone*, b. p. 120—125°/20—21 mm. (10·0 g.) (Found: C, 71·0; H, 9·5. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·5%). The *copper complex* separated from light petroleum (b. p. 60—80°) in green needles, m. p. 165·5° (Found: C, 59·8; H, 7·7. $C_{20}H_{30}CuO_4$ requires C, 60·4; H, 7·5%). The infrared absorption of the diketone was typically conjugate chelate in type. The diketone was soluble in dilute aqueous alkali and gave a deep purple ferric test.

2-Acetyl-2-chloro-4,4-dimethylcyclohexanone (I; R = Me).—Treatment of the foregoing diketone (4·2 g.) in carbon tetrachloride (12 c.c.) with sulphuryl chloride (3·7 g.) in carbon tetrachloride (8 c.c.), in the usual manner, gave *2-acetyl-2-chloro-4,4-dimethylcyclohexanone*, b. p. 138—140°/19 mm. (4·6 g.) (Found: C, 58·9; H, 7·6. $C_{10}H_{15}ClO_2$ requires C, 59·2; H, 7·4%). The product was insoluble in cold, aqueous alkali and gave a negative ferric test. In a liquid film it had CO bands at 1725 and 1745 cm.$^{-1}$, CMe_2 bands at 1393, 1364, 1170, 1142, and 821 cm.$^{-1}$ and a CCl band at 773 cm.$^{-1}$.

Attempts to dehydrochlorinate the product by heating it with collidine gave largely unchanged material. More prolonged treatment at higher temperature gave, at best, 50% of the calculated amount of collidine hydrochloride, accompanied by tar. A trace of alkali-soluble material was obtained; on infrared and chemical evidence this contained some 2-acetyl-4,4-dimethylcyclohexanone.

Dimeric Product,[1] $C_{16}H_{20}O_4$.—The dehydrochlorination of 2-acetyl-2-chlorocyclohexanone has been improved, to yield the crystalline product, $C_{16}H_{20}O_4$, in 20% yield. It crystallised from methanol in rhombic prisms, m. p. 136°.

Hydrolytic Cleavage of the Dimeric Product (XXII).—The crystalline product, $C_{16}H_{20}O_4$ (10 g.), was refluxed with 5% aqueous potassium hydroxide (90 c.c.) for 1½ hr. under nitrogen. The cooled solution was subjected to continuous ether-extraction overnight, and the extract dried and concentrated. The syrupy *tricyclo*[6,2,2,$0^{2,7}$]*dodecane-4,10-dione* distilled at 150—155° (bath)/0·05 mm. (0·6 g.) (Found: C, 74·9; H, 8·5. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·3%), $\nu_{max.}$ (in CCl_4) 1720 cm.$^{-1}$ (CO) (see above). The *disemicarbazone* separated in needles, m. p. 226°, from a large volume of ethanol (Found: N, 26·9. $C_{14}H_{22}N_6O_2$ requires N, 27·4%). The diketone condensed with piperonaldehyde in ethanol, in the presence of 5N-aqueous sodium hydroxide, to yield a *tripiperonylidene derivative*, which crystallised from ethanol in solvated needles, m. p. 212—213° (Found: C, 71·85, 71·8; H, 5·4, 5·4. $C_{26}H_{28}O_5,C_2H_6O$ requires C, 71·9; H, 5·4%), $\nu_{max.}$ (in $CHCl_3$) 3571 cm.$^{-1}$ (OH). A reaction under similar conditions with benzaldehyde yielded a gummy product which could not be purified.

Acidification of the alkaline hydrolysis liquor yielded, after ether-extraction, an acidic syrup which contained acetic acid (*S*-benzylthiouronium salt, m. p. and mixed m. p. 136°). Evaporation of the acetic acid *in vacuo* left a syrupy mixture of keto-acids, which could not be purified or characterised. It gave a positive reaction with Brady's reagent.

Reduction of the Diketone $C_{12}H_{16}O_2$ to the Diol $C_{12}H_{20}O_2$.—The diketone (0·52 g.) in dry ether (20 c.c.) was added gradually to a swirled suspension of lithium aluminium hydride (0·4 g.) in dry ether (15 c.c.). The ethereal suspension was refluxed for 1½ hr. and kept at room temperature overnight. After addition of "Celite" and the minimum quantity of water the ether was decanted, dried, and evaporated. The residual 4,10-*diol* distilled at 155—165°

[18] von Auwers and Keil, *Ber.*, 1902, **35**, 4207.
[19] Miller and Adams, *J. Amer. Chem. Soc.*, 1936, **58**, 787.
[20] von Auwers and Lange, *Annalen*, 1913, **401**, 303.
[21] *Org. Reactions*, Vol. VIII, p. 130.

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(bath)/0·03 mm. (0·48 g.) (Found: C, 73·4, 73·5; H, 10·5, 10·3. $C_{12}H_{20}O_2$ requires C, 73·5; H, 10·2%), $\nu_{max.}$ (in CCl_4) 3642 cm.$^{-1}$ (OH) (no carbonyl band). The *di*-p-*nitrobenzoate* separated from a small volume of benzene in needles, m. p. 209° (Found: N, 5·6. $C_{26}H_{28}N_2O_8$ requires N, 5·7%).

Dehydrogenation of the Diol $C_{12}H_{20}O_2$.—The diol (0·37 g.) and 30% palladised charcoal [22] (0·12 g.) were heated at 300° in a slow current of dry nitrogen for 8 hr. After a few minutes water droplets were noted on the cooler parts of the apparatus. The cooled mixture was leached with methanol, and the solution filtered and concentrated through a short column. The residue (0·2 g.) was steam-distilled, yielding, after isolation with ether, a product, b. p. 70—100°/18 mm. (Found: C, 89·3; H, 9·1. Calc. for $C_{10}H_{12}$ requires C, 90·9; H, 9·1%), with a strong tetralin-like odour, which decolorised acid permanganate solution immediately. The infrared spectrum (liquid film) indicated that the product was a mixture of hydrocarbons, but bands characteristic of an *ortho*-disubstituted benzene system were discernible in the 1600—2000 cm.$^{-1}$ region.

Wolff–Kishner Reduction of the Diketone $C_{12}H_{16}O_2$.—The disemicarbazone (0·48 g.; see above) of the diketone was heated in a sealed tube at 200° for 8 hr. with 98—100% hydrazine hydrate (1 c.c.) and sodium ethoxide, obtained by dissolving sodium (0·75 g.) in ethanol (15 c.c.). The tube was cooled and the contents were poured into a large volume of water. The oil which separated was taken up in ether, and the extract washed with dilute hydrochloric acid and water and dried. Evaporation of the solvent under reduced pressure through a column gave tricyclo[6,2,2,$0^{2,7}$]dodecane, b. p. 107—108°/14 mm., $n_D^{19·5}$ 1·5080 (0·15 g.) (Found: C, 87·6; H, 12·3. Calc. for $C_{12}H_{20}$: C, 87·8; H, 12·2%), identical (infrared comparison) with an authentic specimen (see below).

Tricyclo[6,2,2,$0^{2,7}$]*dodeca-5,9-diene* (XIX): *Dimerisation of Cyclohexa-1,3-diene.*—Cyclohexa-1,3-diene was prepared from cyclohexene by bromination [23] and dehydrobromination.[24] The hydrocarbon was distilled over sodium through a fractionating column packed with a 25 cm. glass spiral, a lower fraction consisting chiefly of a cyclohexa-1,3-diene–ether azeotrope being rejected. The diene had b. p. 80°, $\lambda_{max.}$ (in hexane) 257 mμ (lit.,[25,26] $\lambda_{max.}$ 256 mμ), n_D^{20} 1·4755 (lit.,[25] n_D^{20} 1·4755). Vapour-phase chromatography of the product on "Embacel" moistened with dinonyl phthalate showed it to be substantially free from diethyl ether. Cyclohexa-1,3-diene (3·25 g.) was heated in a sealed tube at 200—220° for 10 hr.[24] The contents of the tube were distilled over sodium, the dimer (1·3 g.) being collected at 100—102°/9 mm., n_D^{22} 1·5260 (lit.,[24] b. p. 86—87°/0·3 mm., n_D^{20} 1·5288). Infrared absorption (liquid film) showed a C=C band at 1656 cm.$^{-1}$ and *cis*-CH=CH– bands at 710 and 3067 cm.$^{-1}$. The dimer gave the reported colour reactions [24] with concentrated sulphuric acid.

Tricyclo[6,2,2,$0^{2,7}$]*dodecane* (XXI).—The foregoing dimeric product (0·48 g.) was shaken in ethanol solution in hydrogen at room temperature and pressure for 4 hr. with pre-reduced Adams platinum oxide (absorption: 2 mols.).[12,14] The catalyst and solvent were removed; the residual tricyclo[6,2,2,$0^{2,7}$]dodecane, distilled over sodium, had b. p. 110—111°/16 mm., n_D^{20} 1·5081 (0·3 g.) (lit.,[14] b. p. 102°/7·5 mm.) (Found: C, 87·5; H, 12·4. Calc. for $C_{12}H_{20}$: C, 87·8; H, 12·2%). The product was identical (infrared comparison) with the hydrocarbon obtained by the Wolff–Kishner reduction of the $C_{12}H_{16}O_2$ diketone (see above).

5,6:9,10-*Diepoxytricyclo*[6,2,2,$0^{2,7}$]*dodecane* (XXV).—A chloroform solution of perbenzoic acid was prepared [27] from benzoyl peroxide (31·1 g. of 70% purity) in dry toluene (300 c.c.) and sodium ethoxide [from sodium (4·6 g.) and absolute ethanol (100 c.c.)] at −15°. Tricyclo[6,2,2,$0^{2,7}$]dodeca-5,9-diene (0·8 g.) (0·005 mol.) was added gradually dropwise, with swirling, to this solution (26 c.c.; 0·0105 mol.) at below 0°, and the mixture was kept at 0° for 48 hr. The chloroform solution was washed in turn with saturated sodium hydrogen carbonate solution and water, dried, and concentrated on the water-bath. The residual *diepoxide* distilled at 96°/0·1—0·2 mm., 88°/0·05 mm. (0·42 g.) (Found: C, 74·8; H, 7·9. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·3%). Its infrared absorption (in CCl_4) showed *cis*-epoxide bands at 829 and 1250 cm.$^{-1}$, but no C=C or hydroxyl bands. The product gave no colour with tetranitromethane.

[22] Linstead and Thomas, *J.*, 1940, 1127.
[23] *Org. Synth.*, 1934, **12**, 26.
[24] Hofmann and Damm, *Mitt. Schleschischen Kohlensforschungsinst. Kaiser-Wilhem Ges.*, 1925, **2**, 97; *Chem. Zentr.*, 1926, I, 2342.
[25] Allsopp, *Proc. Roy. Soc.*, 1934, **143***A*, 618.
[26] Henri and Pickett, *J. Chem. Phys.*, 1939, **7**, 439.
[27] *Org. Synth.*, Coll. Vol. I, 1941, 431.

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An attempt to rearrange the diepoxide to a diketone by using lithium diethylamide [15] was unsuccessful, resinous material and unchanged diepoxide being obtained.

We thank Shell Chemicals, Ltd., for a gift of cyclohexa-1,3-diene and the Imperial Smelting Corporation for a gift of boron trifluoride. We are indebted to Dr. G. Eglinton (University of Glasgow) and Mr. G. Phillips for the infrared data, and to the D.S.I.R. for a maintenance grant (to C. W. T. H.).

DEPARTMENT OF CHEMISTRY,
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684. *The Activation of Carbon–Carbon Double Bonds by Cationic Catalysts. Part X.*[1] *The Reaction between* 1,1,3,3-*Tetraphenylbut-*1-*ene, Antimony Trichloride, and Hydrogen Chloride in Benzene.*

By ALWYN G. EVANS, E. A. JAMES, and E. D. OWEN.

The reaction of 1,1,3,3-tetraphenylbut-1-ene in the presence of antimony trichloride and hydrogen chloride in benzene has been studied by a dilatometric method. No reaction occurs in the absence of hydrogen chloride or in the absence of antimony trichloride. The initial rate of reaction is of the first order in the butene and in hydrogen chloride, and of the third order in antimony trichloride. It proceeds to the equilibrium mixture of 1,1-diphenylethylene and 1,1,3,3-tetraphenylbut-1-ene, which in the presence of large concentrations of antimony trichloride slowly gives 3-methyl-1,1,3-triphenylindane.

The reaction of 1,1-diphenylethylene in the presence of antimony trichloride and hydrogen chloride has also been studied in benzene. It is of the first order in 1,1-diphenylethylene and proceeds to the equilibrium mixture of this with the tetraphenylbutene.

IN earlier parts, the action of cationic catalysts on 1,1-diphenylethylene and its linear dimer, 1,1,3,3-tetraphenylbut-1-ene, has been examined by using a dilatometric method to follow the reaction. We have now extended this work by studying the catalytic action of antimony trichloride–hydrogen chloride on these olefins.

EXPERIMENTAL

Materials.—"AnalaR" antimony trichloride was sublimed several times under a high vacuum, the middle fraction only being retained each time. Finally it was sublimed into calibrated ampoules fitted with magnetically operated breakers and sealed off under a high vacuum. The ampoules were then placed in a water-bath at 75° and when the antimony trichloride melted its volume was measured on the calibrated stem. The density at this temperature being known,[2] the weight was calculated. When solutions of antimony trichloride in benzene were required, it was dissolved in benzene under a high vacuum, to give a stock solution for dilution as required.

1,1,3,3-Tetraphenylbut-1-ene (linear dimer) was prepared and purified as in Part VIII.[3] Hydrogen chloride was prepared as in Part VII.[4] Benzene, purified as in Part VIII,[3] was stored for several months under a high vacuum in vessels fitted with magnetically operated breakers and containing sodium–potassium alloy.

[1] Part IX, Evans and Owen, *J.*, 1959, 4123.
[2] Jager, *Z. anorg. Chem.*, 1917, **101**, 1.
[3] Evans and Price, *J.*, 1959, 2982.
[4] Evans and Lewis, *J.*, 1959, 1946.

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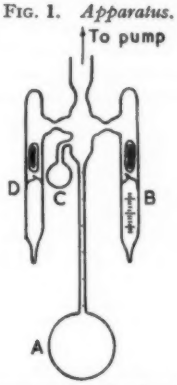
1,1-Diphenylethylene (monomer) was prepared and purified as described in Part V.[5]

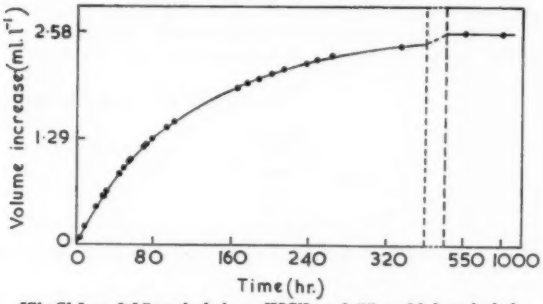
Procedure.—This was the same as described in Part VIII,[3] except that antimony trichloride was used instead of stannic chloride. The apparatus for adding the catalyst to the benzene solution of the olefin is shown in Fig. 1. When small concentrations of antimony trichloride were required, vessel B contained a benzene solution of antimony trichloride, but for high concentrations the solid was used.

FIG. 1. *Apparatus.*



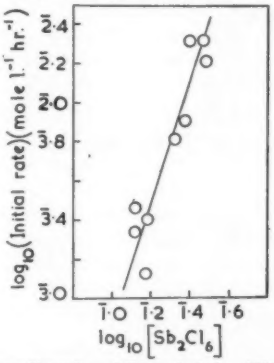
A, *Dilatometer.* B, *Catalyst ampoule.* C, *Optical cell.* D, *Cocatalyst ampoule.*

FIG. 2. *A typical reaction curve.*



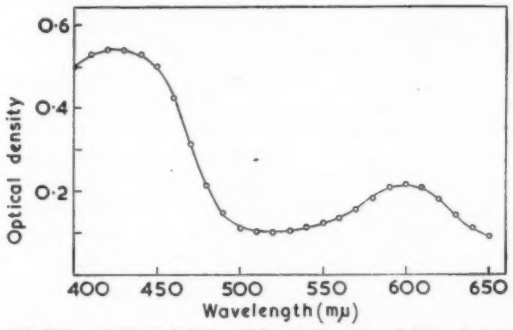
$[Sb_2Cl_6]$ = 0·15 mole l.$^{-1}$. [HCl] = 1·55 × 10^{-3} mole l.$^{-1}$. [Linear dimer] = 0·70 mole l.$^{-1}$. Temp. = 40°.

FIG. 3. *Order in* Sb_2Cl_6 *at* 40°.



[Linear dimer] = 0·78 mole l.$^{-1}$. [HCl] = 2·0 × 10^{-3} mole l.$^{-1}$. Slope = 3.

FIG. 4. *Spectrum of solution. This solution was colourless for the first* 120 *hours after which the colour began to develop.*



$[Sb_2Cl_6]$ = 0·31 mole l.$^{-1}$. [Linear dimer] = 0·78 mole l.$^{-1}$. [HCl] = 2·33 × 10^{-3} mole l.$^{-1}$. Temp. = 40°.

Results.—Orders in reagents. In the absence of hydrogen chloride, dilatometers containing rigorously purified benzene, linear dimer, and antimony trichloride showed no volume change over a period of several weeks. On the introduction of hydrogen chloride the volume increased with time and reached a stationary value (Fig. 2). The expansion observed was, within 5%, that expected for the conversion of linear dimer into the equilibrium mixture of monomer and linear dimer,[5] and hence the values of $\Delta G°$, $\Delta H°$, and $\Delta S°$ for the reaction are the same as those obtained earlier for the stannic chloride–hydrogen chloride system. Initial rates of reaction were found from the initial slopes of the reaction curves, and their dependence on reagent

[5] Evans and Lewis, *J.*, 1957, 2975.

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concentration is shown in Tables 1 and 2 and Fig. 3. It is seen that the order in hydrogen chloride is $1\cdot0 \pm 0\cdot2$, in linear dimer is $1\cdot0 \pm 0\cdot1$, and in antimony trichloride is 3. For systems containing high antimony trichloride concentrations, ($[Sb_2Cl_6] > 0\cdot21$ mole $l.^{-1}$) the stationary period of monomer–linear dimer equilibrium was followed by a slow decrease in volume. Analysis of the solution showed that this decrease was due to the formation of the cyclic dimer, 3-methyl-1,1,3-triphenylindane.

Use of dilatometers containing the monomer, 1,1-diphenylethylene, benzene, antimony trichloride, and hydrogen chloride disclosed a volume decrease with time; when no further change occurred, the contraction was, within 5%, that expected for the conversion of monomer into the monomer–dimer equilibrium mixture.[5] The dependence of initial rate on monomer concentration is shown in Table 3, and it is seen that the order in monomer is $1\cdot0 \pm 0\cdot1$.

Temperature-dependence. The initial rate of conversion of linear dimer into monomer varies over the temperature range 30—55° as shown in Table 4. A plot of $\log_{10}$ (Initial rate/[HCl]) against $1/T$ gives a good straight line from which the activation energy is found to be 11·5 kcal. $mole^{-1}$.

TABLE 1. *Order in* HCl *at* 40°.

[LD] * (mole $l.^{-1}$)	$[Sb_2Cl_6]$ (mole $l.^{-1}$)	[HCl] (10^{-2} mole $l.^{-1}$)	IR * (10^{-3} mole $l.^{-1}$ $hr.^{-1}$)	IR */[HCl] (10^{-2} $hr.^{-1}$)
0·58	0·15	1·16	0·483	4·17
0·58	0·15	1·49	0·650	4·36
0·58	0·15	2·06	1·02	4·95
0·58	0·15	4·05	1·50	3·70

* IR = Initial rate of disappearance of linear dimer in mole $l.^{-1}$ $hr.^{-1}$. LD = Linear dimer.

TABLE 2. *Order in linear dimer at* 40°.

[LD] (mole $l.^{-1}$)	$[Sb_2Cl_6]$ (mole $l.^{-1}$)	[HCl] (10^{-2} mole $l.^{-1}$)	IR (10^{-3} mole $l.^{-1}$ $hr.^{-1}$)	IR/[HCl][LD] (10^{-2} $mole^{-1}$ l. $hr.^{-1}$)
0·373	0·15	1·48	0·406	7·36
0·581	0·15	1·49	0·65	7·53
0·70	0·15	1·55	0·872	8·04

TABLE 3. *Order in monomer at* 40°.

[M] † (mole $l.^{-1}$)	$[Sb_2Cl_6]$ (mole $l.^{-1}$)	[HCl] (10^{-2} mole $l.^{-1}$)	IR † (10^{-4} mole $l.^{-1}$ $hr.^{-1}$)	IR/[M] (10^{-4} $hr.^{-1}$)
1·20	0·14	8·4	9·92	8·24
0·805	0·14	8·4	6·67	8·29
0·56	0·14	8·4	5·08	9·04

† IR = initial rate of appearance of linear dimer in mole $l.^{-1}$ $hr.^{-1}$. M = Monomer.

TABLE 4.

LD (mole $l.^{-1}$)	$[Sb_2Cl_6]$ (mole $l.^{-1}$)	[HCl] (10^{-2} mole $l.^{-1}$)	IR * (10^{-3} mole $l.^{-1}$ $hr.^{-1}$)	Temp.
0·64	0·155	1·79	0·97	30°
0·64	0·155	1·67	1·75	40
0·64	0·155	1·90	4·69	55

* IR = Initial rate of disappearance of linear dimer in mole $l.^{-1}$ $hr.^{-1}$).

Spectra of solutions. Reacting systems were colourless during the period leading to the establishment of the monomer–linear dimer equilibrium. For those systems in which $[Sb_2Cl_6]$ was greater than 0·21 mole $l.^{-1}$, the stationary period of monomer–linear dimer equilibrium was followed after several weeks by a slow decrease in volume as the cyclic dimer was formed, and at this stage the solutions became coloured. For these cases samples of the reaction mixture were sealed off in spectroscopic cells (*D*, Fig. 1), and the spectra were measured (Fig. 4).

DISCUSSION

Mechanism of Reaction.—The results show that antimony trichloride requires a cocatalyst for the activation of olefinic double bonds. With hydrogen chloride as

cocatalyst, both the monomer and the linear dimer react to form the equilibrium mixture of monomer and linear dimer. The initial rate for the reaction of the linear dimer is of the first order in linear dimer and of the first order in hydrogen chloride, but the order in antimony trichloride is three. We believe that this high order is due to the fact that antimony trichloride helps to solvate the ion pairs formed by the addition of a proton to the olefin.

Since the antimony trichloride will most certainly be dimeric under the conditions of our experiments, we will write the following reaction scheme, which is analogous to that given for the reaction catalysed by stannic chloride–hydrogen chloride except that in the latter case the stannic salt did not help to solvate the ion pairs. We shall refer to reactions (*a*) as forward reactions, and to reactions (*b*) as reverse reactions.

$$3Sb_2Cl_6 + HCl + \underset{\text{Monomer}}{CH_2{:}CPh_2} \underset{b}{\overset{a}{\rightleftharpoons}} \{Me{\cdot}C^+Ph_2\ Sb_2Cl_7^-\}_{2Sb_2Cl_6} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ (1)$$

$$\{Me{\cdot}C^+Ph_2\ Sb_2Cl_7^-\}_{2Sb_2Cl_6} + CH_2{:}CPh_2 \underset{b}{\overset{a}{\rightleftharpoons}} \{Me{\cdot}CPh_2{\cdot}CH_2{\cdot}C^+Ph_2\ Sb_2Cl_7^-\}_{2Sb_2Cl_6} \quad \ldots\ldots\ (2)$$

$$\{Me{\cdot}CPh_2{\cdot}CH_2{\cdot}C^+Ph_2\ Sb_2Cl_7^-\}_{2Sb_2Cl_6} \underset{b}{\overset{a}{\rightleftharpoons}} \underset{\text{Linear dimer}}{Me{\cdot}CPh_2{\cdot}CH{=}CPh_2} + 3Sb_2Cl_6 + HCl \quad \ldots\ldots\ (3)$$

That the initial rate for the conversion of monomer into linear dimer is of the first order in monomer shows that the rate-determining step in the forward direction is reaction (1*a*). One would thus expect that the rate-determining step for the reverse reaction would be (1*b*). If this were so, the initial rate of the reverse reaction would depend on [linear dimer]$^{\frac{1}{2}}$, whereas in fact, it depends on [linear dimer],[1] which would require reaction (2*b*) to be the rate-determining step. We believe the explanation of these results to be as follows.

The orders in the reagents have been obtained from the initial rates of the forward and the reverse reactions. At zero time, the concentration of monomer will be equal to [initial monomer] for the forward reaction, but will be equal to zero for the reverse reaction. Thus the monomer ion, when formed from the monomer by reaction (1*a*), in the initial stages of the forward reaction, can undergo rapid conversion into the dimer ion by reaction (2*a*) because there will be a high concentration of monomer present, and the rate-determining step for the initial stages of the forward reaction will be reaction (1*a*). When the monomer ion is formed from the dimer ion by reaction (2*b*) in the initial stages of the reverse reaction, however, its conversion back into the dimer ion will be much slower because the concentration of monomer present will be negligibly small. Its reaction to monomer by reaction (1*b*), however, is independent of monomer concentration, and, hence, at these negligibly small monomer concentrations, every monomer ion produced by reaction (2*b*) will undergo conversion into monomer by reaction (1*b*). That is, the rate-determining step for the initial stages of the reverse reaction will be reaction (2*b*).

Thus we may write:

$$\text{Initial rate of forward reaction} = k_f[M][HCl][Sb_2Cl_6]^3,$$
$$= k_{1a}[M][HCl][Sb_2Cl_6]^3,$$
$$i.e.,\ k_f = k_{1a}.$$

$$\text{Initial rate of reverse reaction} = k_r[LD][HCl][Sb_2Cl_6]^3$$
$$= \frac{k_{2b}k_{3b}}{k_{3a}} \cdot [LD][HCl][Sb_2Cl_6]^3,$$
$$i.e.,\ k_r = k_{2b}k_{3b}/k_{3a},$$

where M = monomer, and LD = linear dimer.

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Thermodynamic Quantities for the Reaction.—In Table 5 we give the thermodynamic results for the reaction of linear dimer to monomer (reverse reaction). It is seen that the large amount of solvation of the ions has reduced $\Delta H_r^{\ddagger}$ to quite a low value; in fact it is only 0·6 kcal. mole^{-1} greater than the value of ΔH_r° (10·3 kcal. mole^{-1}), the endothermicity of the reverse reaction.

TABLE 5. *Results for the conversion of linear dimer into monomer (reverse reaction).*

k_r * 1·4	$\Delta G_r^{\ddagger}$ 21·0 (40°) ΔG_r° 1·55 (39·9°) †	$\Delta H_r^{\ddagger}$ 10·9 ΔH_r° 10·3 †	$\Delta S_r^{\ddagger}$ −32·3 (40°) ΔS_r° 28·0 (39·9°) †
(10^{-3} mole^{-4} l.^{4} sec.$^{-1}$)	(kcal. mole^{-1})	(kcal. mole^{-1})	(cal. deg.$^{-1}$ mole^{-1})

* Obtained from Fig. 3. † Obtained from results for forward reaction.[4]

Formation of Cyclic Dimer.—When [Sb_2Cl_6] is less than 0·21 mole l.$^{-1}$, the monomer–linear dimer equilibrium is reached without a colour developing and no further change occurs during 12 months. When [Sb_2Cl_6] exceeds 0·21 mole l.$^{-1}$, the equilibrium mixture undergoes a very slow change to cyclic dimer. For example, when [Sb_2Cl_6] = 0·3 mole l.$^{-1}$, [linear dimer] = 0·78 mole l.$^{-1}$, and [HCl] = 2·33 × 10^{-2} mole l.$^{-1}$, the monomer–linear dimer equilibrium is attained in 20 hours, and the dilatometer reading remains constant for a further 100 hours, after which the volume very slowly decreases, a colour develops, and analysis shows that cyclic dimer is being formed. Thus it is seen that for antimony trichloride–hydrogen chloride systems, the rate at which linear dimer is converted into cyclic dimer is very much slower than its rate of conversion into monomer.

Spectrum of Solution.—The antimony trichloride–hydrogen chloride catalyst differs from all those which we have used previously for this reaction, in that it brings about the monomer–linear dimer equilibration without the solution's showing the characteristic spectrum of the carbonium ion. This must mean that the ion pair, consisting of the carbonium ion and the $Sb_2Cl_7^-$ counter-ion and solvated by antimony trichloride, is much more unstable than the ion pairs obtained in the other catalytic systems we have studied.

For those systems in which [Sb_2Cl_6] exceeds 0·21 mole l.$^{-1}$, we find that, although no colour is present in the solution during the attainment of the monomer–linear dimer equilibrium, and for the stationary period of this equilibrium, a colour develops as the solution undergoes the further contraction to form cyclic dimer. This colour (see Fig. 4) is characteristic of the monomer in a weak acid medium;[6] it is not due to the formation of cyclic dimer, since the system cyclic dimer–antimony trichloride–hydrogen chloride is colourless and shows no change in volume with time.

It appears that there is a slow increase in the number of antimony trichloride molecules solvating the ion pairs, the final extent of solvation being greater the greater the antimony trichloride concentration. Monomer–linear dimer equilibration can occur at reasonable rates for a degree of solvation which is, however, not sufficient to give a concentration of ion pairs which is visible. When [Sb_2Cl_6] is greater than 0·21 mole l.$^{-1}$, the monomer–linear dimer equilibration is completed during the early stages of the ion-pair solvation. However, solvation continues slowly until the ion-pair concentration is high enough to be visible, and at this stage the concentration of linear dimer ions is also high enough for them to be converted into cyclic dimer by reaction (4) at a measurable, though extremely slow, rate. We found earlier, for the stannic chloride–hydrogen chloride system,[3] that cyclisation of the linear dimer ion is associated with a large negative entropy term, and much higher concentrations of linear dimer ion are required in order to obtain a reasonable rate of conversion of linear dimer into cyclic dimer than are necessary for its conversion into monomer.

$$\{Me{\cdot}CPh_2{\cdot}CH_2{\cdot}C^{+}Ph_2\ Sb_2Cl_7^{-}\}_{(n-1)Sb_2Cl_6} \longrightarrow \underset{CPh_2}{\overset{Me{\cdot}PhC\!\!-\!\!CH_2}{\text{cyclic dimer}}} + nSb_2Cl_6 + HCl \quad . \quad . \quad (4)$$

$n > 3$

[6] Evans, Jones, and Thomas, *J.*, 1957, 104.

Since the initial rate of conversion of linear dimer into monomer can depend on antimony trichloride concentration to as high an order as 3 without the solution's being coloured, it seems that when the colour finally becomes visible the ion pairs must be enclosed in very many molecules of antimony trichloride, almost as though they are in a medium of liquid antimony trichloride. It is interesting, in this connexion, that in the absence of benzene—that is, in liquid antimony trichloride at its melting point (73°)—the reaction solutions are intensely coloured immediately they are made up.

We thank Dr. J. L. Cotter for help with the initial part of this work, and The Distillers Company Ltd. for financial help. One of us (E. A. J.) thanks the D.S.I.R. for a Research Studentship.

UNIVERSITY COLLEGE, CARDIFF. [*Received, February 21st,* 1961.]

NOTES.

685. *Organic Fluorine Compounds. Part XXIII.* Methylene Reactivity in Ethyl Fluoroacetate.*

By ERNST D. BERGMANN and S. COHEN.

SINCE ethyl fluoroacetate enters Claisen reactions [1,2] and condenses with aromatic aldehydes,[3] and the sodium derivative of its enol can be used for alkylation [4] and acylation,[2,5] we have studied the reaction of aliphatic ketones with the enol of this ester. Acetone and ethyl methyl ketone afford simultaneously the two possible products. Acetone gave 14% of ethyl α-fluoro-β-hydroxy-β-methylbutyrate and 34% of 1-fluoropentane-2,4-dione;[6] ethyl methyl ketone gave 14% of ethyl α-fluoro-β-hydroxy-β-methylvalerate and 20% of 1-fluorohexane-2,4-dione, whose structure is assumed by analogy with the reaction between ethyl acetate and ethyl methyl ketone. Ethyl α-fluoro-β-hydroxy-β-methylbutyrate had been obtained by the Reformatzky reaction between acetone and ethyl chlorofluoroacetate;[8] the analogous synthesis with ethyl methyl ketone is described in this paper.

The sodium derivative of the enol of ethyl fluoroacetate failed to enter Michael reactions, but with chloral gave a mixture of isomers of ethyl γγγ-trichloro-α-fluoro-β-hydroxybutyrate.

Experimental.—Ethyl α-fluoro-β-methyl-β-hydroxyvalerate and 1-fluorohexane-2,4-dione. To a stirred suspension of sodium hydride (12 g.) in ether (100 ml.), a solution of ethyl fluoroacetate (53 g.) and ethyl methyl ketone (36 g.) in ether (100 ml.) was added dropwise at 0°. Stirring was continued for 1 hr. after the mixture had become homogeneous. The brown solution was poured on ice and sulphuric acid, and the organic layer separated, dried, and distilled, giving *1-fluorohexane-2,4-dione* (13 g., 20%), b. p. 65—68°/33 mm. (Found: C, 54·7; H, 7·0; F, 14·5. $C_6H_9FO_2$ requires C, 54·6; H, 6·8; F, 14·4%), and *ethyl α-fluoro-β-hydroxy-β-methylvalerate* (13 g., 14·5%), b. p. 67—69°/2 mm. (Found: C, 53·6; H, 8·6; F, 10·6. $C_8H_{15}FO_3$ requires C, 53·9; H, 8·4; F, 10·7%), $\nu_{max.}$ (liquid film) 3420 (OH), 1740 (C=O), 1085, and 1030 (C–F) cm.$^{-1}$. The *cupric salt* of the diketone recrystallised from ethanol as light blue needles, decomp. >250° (Found: F, 11·9. $C_{12}H_{16}CuF_2O_4$ requires F, 11·7%).

The ethyl ester (10 g.) was refluxed on the steam-bath for 30 min. with acetic acid (10 ml.)

* Part XXII, *J.*, 1961, 3457.

[1] Blank, Mager, and Bergmann, *J.*, 1955, 2190.
[2] Bergmann, Cohen, and Shahak, *J.*, 1959, 3278.
[3] Bergmann and Schwarcz, *J.*, 1956, 1524.
[4] Bergmann and Szinai, *J.*, 1956, 1521.
[5] Bergmann, Cohen, and Shahak, *J.*, 1959, 3286.
[6] Fackler and Cotton, *J.*, 1960, 1435.
[7] Levine, Conroy, Adams, and Hauser, *J. Amer. Chem. Soc.*, 1945, **67**, 1510.
[8] Bergmann, Cohen, Hoffman, and Rand-Meir, *J.*, 1961, 3457.

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and hydrochloric acid (20 ml.). Distillation gave the *acid* (4 g., 48%), b. p. 105—108°/0·2 mm., m. p. 87—90° (Found: F, 12·9. $C_6H_{11}FO_3$ requires F, 12·7%).

To a suspension of magnesium amalgam [from magnesium turnings (5 g.) and mercury (2 g.) in hot toluene (50 ml.)] a solution of ethyl chlorofluoroacetate [9] (29 g.) and ethyl methyl ketone (14·4 g.) in toluene (50 ml.) was added dropwise. An exothermic reaction took place, whereupon the external heating was discontinued. The mixture was refluxed for 1 hr. and poured on ice and sulphuric acid, and the organic layer was separated, dried, and distilled. The ester, b. p. 62—63°/1 mm. (15 g., 42%), was hydrolysed with acetic acid and hydrochloric acid as described above, and the acid identified with the above product by analysis and mixed m. p. (Found: C, 47·7; H, 7·7; F, 12·8. Calc. for $C_6H_{11}FO_3$: C, 48·0; H, 7·3; F, 12·7%), $\nu_{max.}$ (in KBr) 3400 (OH), 1735 (C=O), in the C–F region 1070, 1060, 1030, 1010 cm.$^{-1}$.

Ethyl α-fluoro-β-hydroxy-β-methylbutyrate and 1-fluoropentane-2,4-dione. Analogously, acetone (29 g.) gave 1-fluoropentane-2,4-dione (20 g., 34%), b. p. 50—52°/27 mm. (Found: F, 15·5. Calc. for $C_5H_7FO_2$: F, 16·1%), and ethyl α-fluoro-β-hydroxy-β-methylbutyrate (11 g., 13·5%), b. p. 47—49°/0·5 mm. (Found: C, 51·5; H, 7·5; H, 11·1. Calc. for $C_7H_{13}FO_3$: C, 51·2; H, 8·0; F, 11·6%), $\nu_{max.}$ (liquid film) 1730 (C=O; sh 1740), 1600, 1060 (C–F) cm.$^{-1}$.

The *cupric salt* of the diketone formed blue needles, decomp. >250°, from ethanol (Found: C, 40·1; H, 4·1; F, 13·1. $C_{10}H_{12}CuF_2O_4$ requires C, 40·3; H, 4·0; F, 12·6%).

The ester (10 g.) was refluxed with acetic acid (10 ml.) and hydrochloric acid (20 ml.), as described above. The *acid* (3·5 g., 42%) had b. p. 100—110°/0·5 mm., m. p. 68—70° (Found: C, 44·4; H, 6·6; F, 13·5. $C_5H_9FO_3$ requires C, 44·1; H, 6·6; F, 13·9%), $\nu_{max.}$ (in KBr) 3390 (OH), 1740 (C=O), 1020 and 1015 (C–F) cm.$^{-1}$.

Ethyl γγγ-trichloro-α-fluoro-β-hydroxybutyrate. To the sodium derivative of ethyl fluoroacetate [from ethyl fluoroacetate (53 g.) and sodium hydride (12 g.) in dry ether (30 ml.)], chloral (74 g.) was added with cooling and stirring. After 3 hr. the clear solution was decomposed with ice and hydrochloric acid. The ester (20 g., 16%) boiled at 155—160°/2 mm. and solidified. Recrystallisation from toluene gave a product of correct analysis, but with m. p. 70—100°, presumably a mixture of isomers (Found: C, 29·1; H, 3·3. Calc. for $C_6H_8Cl_3FO_3$: C, 28·5; H, 3·2%).

This investigation has been supported by the U.S. National Institutes of Health.

ISRAEL INSTITUTE OF BIOLOGICAL RESEARCH,
NESS-ZIONA. [*Received, January 5th*, 1961.]

[9] Young and Tarrant, *J. Amer. Chem. Soc.*, 1948, **71**, 2432.

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686. *The Colouring Matter of* Rhus cotinus *Wood (Young Fustic).*

By H. G. C. KING and T. WHITE.

SINCE the discovery [1] of fisetin (3,7,3′,4′-tetrahydroxyflavone) in the wood of *Rhus cotinus* in 1886, it has been assumed that the dyeing properties of young fustic extract were due to this flavone. Re-investigation of the wood has now shown that it contains also a significant amount of the aurone sulphuretin (2-benzylidene-6,3′,4′-trihydroxycoumaran-3-one), and a small proportion of a sulphuretin glucoside. An alkaline solution of sulphuretin is deep orange-red; an alkaline solution of fisetin is deep yellow; and it is probable that sulphuretin contributes more significantly than fisetin to the dyeing ability of fustic extract.

Experimental.—Coarsely ground chips of *Rhus cotinus* wood were extracted with ethyl acetate, and the extract was examined by two-dimensional paper chromatography in the solvent systems (1) t-butyl alcohol–acetic acid–water (14 : 25 : 61), and (2) butan-2-ol–acetic acid–water (14 : 1 : 5). Examination under ultraviolet light showed that in addition to fisetin, which fluoresced bright yellow, two components having a dull yellow-green fluorescence were present. Exposing the paper to ammonia vapour changed the last two fluorescences to bright orange, a behaviour characteristic of certain hydroxychalcones and aurones. The R_F values

[1] Schmid, *Ber.*, 1886, **19**, 1734.

of the major component, and its ultraviolet spectrum (after elution from the paper with ethanol) were identical with those of synthetic sulphuretin [2] (in ethanol, $\lambda_{max.}$ 395—397 mμ; 460 mμ in 0·002M-sodium ethoxide). Comparison of the optical density of the compound with that of a standard solution of sulphuretin at 395 mμ indicated that the material extracted with ethyl acetate contained 7·4% of sulphuretin, corresponding to 0·5% in the initial whole wood.

Sulphuretin was then isolated by refluxing the whole extract with ethyl acetate (~50 vol.) and filtering off the undissolved crude aurone. Removal of the contaminating fisetin was difficult and after two recrystallisations from ethanol–water the orange sulphuretin melted at 293° (Found, in product dried at room temperature over P_2O_5: C, 63·1; H, 4·1. Calc. for $C_{15}H_{10}O_5,H_2O$: C, 62·4; H, 4·2%). The triacetyl derivative had m. p. and mixed m. p. 169°.

The minor aurone component was eluted from several chromatograms with ethanol. With ferric chloride solution the solution gave a bright green colour. After being concentrated, it was hydrolysed with 3·7% w/v hydrochloric acid and the hydrolysate examined by paper chromatography with the above solvent system for the aglycone and t-butyl alcohol–ethyl methyl ketone–water (5 : 12 : 3) for the sugar component. Sulphuretin and glucose were the sole hydrolysis products.

The presence of sulphuretin was also demonstrated by chromatography of the wood of *Rhus succedanea*, another species rich also in fisetin.

The authors thank Dr. T. Swain for valuable discussions, and La Compagnie Française des Extraits Tinctoriaux et Tannants, Le Havre, France, for a gift of *Rhus cotinus* wood.

FORESTAL CENTRAL LABORATORIES, HARPENDEN, HERTS.
[Present addresses: see p. 3234.] [*Received, January 18th*, 1961.]

[2] Nordström and Swain, *Arch. Biochem. Biophys.*, 1956, **60**, 329.

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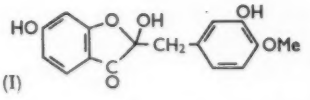
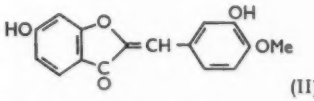
687. *The Reaction of Certain* C_{15} *Compounds with Acetic Anhydride–Sulphuric Acid.*

By H. G. C. KING and T. WHITE.

DURING an investigation of the crystalline 2-benzyl-2,6,3′-trihydroxy-4′-methoxycoumaran-3-one (I) isolated from commercial Quebracho tannin extract,[1] it was found that addition of a drop of concentrated sulphuric acid to a dilute solution of the compound in cold acetic anhydride gave an immediate intense cherry-red colour. An identical reaction was given by the related 2-benzylidene-6,3′-dihydroxy-4′-methoxycoumaran-3-one (II), suggesting that for the hydroxy-compound loss of the elements of water precedes the colour reaction.



(I)



(II)

A series of C_{15} compounds was, therefore, investigated to determine what other structures might exhibit similar colour formation under these conditions. Table 1 shows the results and may be of value in indicating the type of structure present in naturally occurring members of the C_{15} series.

Where the overall structure is chromogenic, successive substitution of methoxy- or benzyloxy-groups for hydroxy-groups leads to intensification of the colour accompanied by a change from yellow through red (partially substituted) to purple (fully methylated), but the specific structure responsible for colour production is not entirely clear. The presence of a double bond conjugated to a keto-group as part of a chain is a contributory factor (*e.g.*, aurones and chalcones), and here elimination of the double bond by reduction or bromination eliminates the colour reaction. In the case of the 2-benzyl-2-hydroxycoumaran-3-ones, removal of the elements of water from the $>C(OH)\cdot CH_2-$ portion of the

[1] King and White, (*a*) *Proc. Chem. Soc.*, 1957, 341; (*b*) *J.*, 1961, 3234.

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TABLE 1. *Colours produced from* C_{15} *compounds* (2 mg.) *in a* 200 : 1 v/v *mixture* (10 ml.) *of acetic anhydride and sulphuric acid.*

Aurones	
6,3′,4′-Trihydroxy-	Orange
6,3′-Dihydroxy-4′-methoxy-	Cerise
6,4′-Dihydroxy 3′-methoxy-	Bright red
6,3′,4′-Trimethoxy-	Purple
2,3-Dihydro-6,3′-dihydroxy-4′-methoxy-	None
2,α-Dibromo-6,3′,4′-trimethoxy-	None
Flavones	
3,7,3′,4′-Tetrahydroxy-	Yellow
3,7,3′-Trihydroxy-4′-methoxy-	Yellow
3-Hydroxy-7,3′,4′-trimethoxy-	Deeper yellow
7-Hydroxy-3,4′-dimethoxy-	Deeper yellow
2,3-Dihydroflavonols	
3,5,7,3′,4′-Pentahydroxy-	None
3,7,3′,4′-Tetrahydroxy-	None
Flavanols	
3,5,7,3′,4′-Pentahydroxy-	None
3-Hydroxy-5,7,3′,4′-tetramethoxy-	Faint yellow
Flavanones	
7,3′-Dihydroxy-4′-methoxy-	Deep pink
7,3′-Dibenzyloxy-4′-methoxy-	Cerise
7,3′,4′-Trimethoxy-	Purple
Chalcones	
3,4,4′-Trihydroxy-	Orange
3,4′-Dihydroxy-4-methoxy-	Cerise
3,4,4′-Tribenzyloxy-	Red
3,4,4′-Trimethoxy-	Purple
2-Benzyl-2-hydroxycoumaran-3-ones	
Unsubstituted	Yellow
6,3′,4′-Trihydroxy-	Orange
6,3′-Dihydroxy-4′-methoxy-	Cerise
6,3′,4′-Trimethoxy-	Purple

molecule produces the corresponding aurone [1b] and therefore results in colour formation. In the flavone family the presence of the double bond does not entail colour formation in this reaction. In the flavanols, loss of water from the ·CH·CH(OH) grouping (if it occurs under these conditions) fails to lead to colour formation, presumably since there is no 4-carbonyl group. The reason for colour formation in the flavanones is not clear since the compounds are fully saturated and cannot lose water under these conditions. It is possible, however, that small amounts of contaminating chalcones were present in the samples tested (flavanones being formed from chalcones by treatment with mineral acid). Chalcones are so sensitive to the reaction that the presence of very small quantities could give a positive colour reaction.

The effects of substitution in altering the colour and in increasing its intensity are shown quantitatively in Table 2.

TABLE 2.

Compound	$\lambda_{max.}$ (mμ)	$E^{1\%}_{1\,cm.}$	Compound	$\lambda_{max.}$ (mμ)	$E^{1\%}_{1\,cm.}$
Aurones			*Aurones*		
6,3,4′-Trihydroxy-	325	730	6,3′,4′-Trimethoxy-	315	205
	375	795		365	115
	420—440	95		424	158
6,4′-Dihydroxy-3′-methoxy-	375	695		570	2240
	450	90	*Coumaran-3-ones*		
6,3′-Dihydroxy-4′-methoxy-	320	257	2-Benzyl-2,6,3′-dihydroxy-4′-methoxy-	380	64
	378	360		540	158
	540	590	2-Benzyl-2,6,3′,4′-tetrahydroxy-	315	138
6-Hydroxy-3′,4′-dimethoxy-	347	190		370—375	58
	560	>1000			

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[Present addresses: see p. 3234.]

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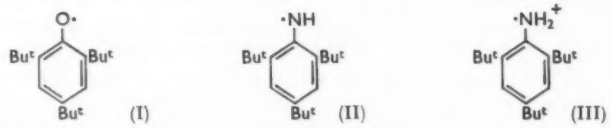
688. *A Stable Anilino-radical.*

By E. J. LAND and G. PORTER.

THE well-known blue radical (I),[1] derived from 2,4,6-tributylphenol, owes its stability to resonance and steric hindrance towards dimerisation or attack on the benzene nucleus. It can be prepared by chemical or photochemical oxidation of this phenol and is stable almost indefinitely in n-hexane solution if all dissolved oxygen is removed. We have prepared the corresponding anilino-radical (II) by photochemial oxidation of a

[1] Cook and Woodworth, *J. Amer. Chem. Soc.*, 1953, **75**, 6242, and subsequent papers; Muller and Ley, *Ber.*, 1954, **82**, 922, and subsequent papers.

thoroughly outgassed 10^{-4}M-solution of 2,4,6-tri-t-butylaniline in n-hexane and cyclohexane with 1000 Joule flashes from a flash-photolysis apparatus. The pink radical solutions so prepared can be preserved for several days when the solvent is n-hexane but



the stability is less in cyclohexane. The radical has a sharp absorption maximum at 3250 Å and much weaker absorption around 4100 Å (Fig. 1); this spectrum is very similar to that of the short-lived anilino-radical $C_6H_5{\cdot}NH{\cdot}$ observed during flash-photolysis of

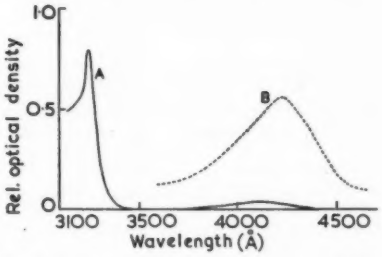
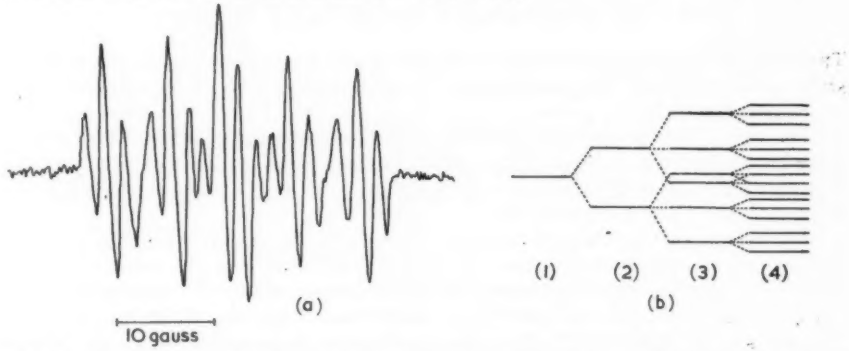


FIG. 1. *Ultraviolet and visible absorption spectra of* (A) *radical* (II) *(in n-hexane) and* (B) *radical* (III) *(in carbon tetrachloride).*

FIG. 2. (a) *Derivative of electron spin resonance spectrum of* (II) *(in n-hexane).* (b) *Energy level system of radical* (II). (1) *Electronic level;* (2) *interaction with* H *on* N *atom;* (3) *interaction with* N *atom;* (4) *interaction with two symmetrical* H *atoms on aromatic ring.*



aniline in the gas phase [2] and in fluid solution [3] or by continuous irradiation in rigid glasses [4] at liquid-nitrogen temperature. Attempts to detect the radical (II) produced chemically by oxidising the amine with lead dioxide, alkaline potassium ferricyanide, or benzoyl peroxide and following the change in ultraviolet absorption above 3000 Å have not been definitely successful, possibly owing to the difficulty of completely removing molecular oxygen occluded by the oxidising agent.

The derivative of the electron spin resonance absorption spectrum of the radical (II) in n-hexane solution of unknown concentration is shown in Fig. 2. It consists of four sets of 1,2,1 triplets, two each side of a 1,3,3,1 quadruplet and the splitting is attributed to interaction of the unpaired electron spin with the nitrogen atom, the hydrogen atom attached to the nitrogen, and the two hydrogen atoms on the aromatic ring. The probable energy

[2] Porter and Wright, *Trans. Faraday Soc.*, 1955, **51**, 1469.
[3] Land and Porter, unpublished work.
[4] Porter and Strachan, *Trans. Faraday Soc.*, 1958, **54**, 1595.

XUM

level system giving rise to this hyperfine pattern is also shown in Fig. 2. N-Proton, N-nucleus, and aromatic proton splitting are 11·9, 6·9, and 1·9 ± 0·2 gauss, respectively. The corresponding N-proton and N-nucleus splittings for the more localised electron in NH_2 are 24·0 and 10·3 gauss.[5]

The equilibrium between the uncharged single anilino- and the charged anilino-radical cation $C_6H_5{\cdot}NH_2^+$ can be followed by flash-photolysis of aqueous aniline solutions of differing pH's.[3] Both appear together in varying relative amounts between pH 4 and 8, only $C_6H_5{\cdot}NH{\cdot}$ being seen at pH 8 and only $C_6H_5{\cdot}NH_2^{+}{\cdot}$ below pH 4. Unfortunately the sterically hindered aniline is very insoluble in water and so the same conditions cannot be used to follow the equilibrium between anilino-form (II) and its protonated form (III). However, a solution of tri-t-butylaniline in carbon tetrachloride or 1 : 1 aqueous ethanol also produces a transient absorption very similar in shape and position to that of $C_6H_5{\cdot}NH_2^{+}{\cdot}$, and we therefore assign this absorption to the protonated hindered radical (III) (Fig. 1).

We are grateful to Dr. W. R. Remington of the Du Pont de Nemours Co. Inc., Delaware, U.S.A. for supplying us with 1 g. of 2,4,6-tri-t-butylaniline, and to Dr. J. K. Brown and Mr. D. Pooley of the Chemistry Department, University of Birmingham, for measuring the electron spin resonance spectrum of the radical, and for a helpful discussion.

THE UNIVERSITY, SHEFFIELD. [*Received, February 16th*, 1961.]

[5] Foner, Cochran, Bowers, and Jen, *Phys. Rev. Letters*, 1958, **1**, 91.

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689. *The Structure of "Boyd's Chloride" (Triphenylmethylphosphonic Dichloride).*

By M. HALMANN, L. KUGEL, and S. PINCHAS.

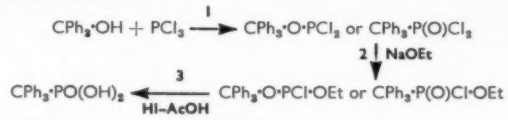
TRIPHENYLMETHANOL reacts readily with phosphorus trichloride to give a well crystallised stable product named "Boyd's chloride."[1-5] This synthesis has been repeatedly quoted as a "curious reaction."[4]

The structure to be expected from the method of preparation is that of triphenylmethyl phosphorodichloridite, $CPh_3{\cdot}O{\cdot}PCl_2$, which agrees with its elementary composition. However, the isomeric structure, $CPh_3{\cdot}P(O)Cl_2$, that of triphenylmethylphosphonic dichloride, must also be considered.

Arguments for the preferred structure of Boyd's chloride, or of its phenyl-substituted derivatives, have been based thus far only on the nature of the products formed by solvolysis. Boiling water hydrolyses the chloride very slowly to triphenylmethanol and phosphorous acid:[5] $CPh_3{\cdot}O{\cdot}PCl_2 + 3H_2O \longrightarrow CPh_3{\cdot}OH + P(OH)_3 + 2HCl$. This reaction seems to favour the phosphorodichloridite structure in which the phosphorus atom is in the tervalent state and on hydrolysis would form phosphorous acid. On the other hand, heating Boyd's chloride with alcoholic alkali[2-5] yields a half ester which is hydrolysed by a concentrated solution of hydriodic acid in acetic acid to a dibasic acid, triphenylmethylphosphonic acid, $CPh_3{\cdot}PO_3H_2$. This acid cannot have the structure $CPh_3{\cdot}O{\cdot}P(O)H{\cdot}OH$, since this belongs to a monobasic acid.[1b] Thus during the reactions (1)—(3) the triphenylmethyl group migrates from oxygen to phosphorus. Previous results, however, have not proved conclusively whether this rearrangement occurs before or after

[1] (*a*) Boyd and Chignell, *J.*, 1923, **123**, 813; (*b*) Boyd and Smith, *J.*, 1924, **125**, 1477.
[2] Hatt, *J.*, (*a*) 1929, 2412; (*b*) 1933, 776.
[3] Hardy and Hatt, *J.*, 1952, 3778.
[4] Kosolapoff, "Organophosphorus Compounds," J. Wiley and Sons, New York, 1950, pp. 64, 70, 125; Van Wazer, "Phosphorus and its Compounds," Interscience Publ. Inc., New York, 1958, pp. 233, 264.
[5] Arbusov and Arbusov, *J. Russ. Phys. Chem. Soc.*, 1929, **61**, 217; Arbusov and Nikonorov, *Zhur. obshchei Khim.*, 1947, **17**, 2129.

the formation of the dichloride, although a phosphonic dichloride structure seemed to fit the chemical reactions better.[2b]



The infrared absorption of Boyd's chloride has now been measured in chloroform and carbon disulphide solutions and compared with published data for several other phosphonic dichlorides, as listed in the Table. A phosphonic dichloride structure requires a strong

Phosphoryl stretching vibration (cm.$^{-1}$) *of various phosphonic dichlorides*, R·P(O)Cl_2.

Compound	Frequency	Solvent	Ref.	Compound	Frequency	Solvent	Ref.
Me·$POCl_2$ ...	1268	CS_2	6	Ph·$POCl_2$ ...	1275	Homog.	7
Et·$POCl_2$ ...	1278	CS_2	6	C_6H_{11}·$POCl_2$	1274, 1258	CS_2	8
Pr^i·$POCl_2$ ...	1248, 1282	CS_2	6	NMe_2·$POCl_2$	1268	Homog.	9
CPh_3·$POCl_2$	1266	CS_2	This work	,,	1269	CCl_4	10
,,	1255	$CHCl_3$	,,				

absorption band at about 1270 cm.$^{-1}$ due to the P=O stretching vibration.[11] The phosphorodichloridite structure must lack such an absorption * and instead show a strong P–O–C stretching band in the 990—1050 cm.$^{-1}$ range.[7,11]

The solutions of Boyd's chloride show a strong absorption band in the 1270 cm.$^{-1}$ region which is typical of phosphonic dichlorides. No strong absorption in the P–O–C stretching region was observed. It can therefore be concluded that Boyd's chloride is indeed triphenylmethylphosphonic dichloride. The somewhat lower P=O stretching frequency of the chloride in chloroform solution (1255 cm.$^{-1}$) than in carbon disulphide (1266 cm.$^{-1}$) must be attributed to the hydrogen bonding [7] existing between the polarised P–O group and the polar H–CCl_3 solvent molecules, by analogy with a similar decrease of the C=O stretching frequency.[13]

The rearrangement during its formation is not as surprising as it seemed thirty years ago. The strong yellow colour of the reaction mixture suggests the presence of the triphenylmethyl cation. The probable reaction sequence is thus:

$$CPh_3{\cdot}OH + PCl_3 \longrightarrow [CPh_3{\cdot}PCl_3]^+OH^- \longrightarrow CPh_3{\cdot}P(O)Cl_2 + HCl$$

in which the carbonium ion is " solvated " by the electron-donating phosphorus trichloride. The subsequent decomposition is analogous to the rearrangement of benzyl-containing phosphonium hydroxides: [14]

$$[PR_3{\cdot}CH_2Ph]^+OH^- \longrightarrow R_3PO + Ph{\cdot}CH_3$$

It is still unknown whether formation of Boyd's chloride is a one-step displacement of the chlorine by an oxygen atom or whether it involves a quinquecovalent phosphorus intermediate.

Experimental.—Triphenylmethylphosphonic dichloride was prepared as described; [3] purified by dissolution in benzene and precipitation with ether (3 times), it had m. p. 188—189° (Found:

* Although the triphenylmethyl group was also observed [11] to show a band at about 1280 cm.$^{-1}$, this group cannot be expected to bring about a strong absorption in this region, since this band was always found to be very weak.

[6] Gerding and Maarsen, *Rec. Trav. chim.*, 1957, **76**, 481.
[7] Daasch and Smith, *Analyt. Chem.*, 1951, **23**, 853.
[8] Bellamy and Beecher, *J.*, 1952, 475.
[9] Harvey and Mayhood, *Canad. J. Chem.*, 1955, **33**, 1552.
[10] Holmstedt and Larsson, *Acta Chem. Scand.*, 1951, **5**, 1179.
[11] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen & Co., London, 1948, p. 311.
[13] Pinchas and Samuel, *J.*, 1954, 863.
[13] Jones and Sandorfy in " Technique of Organic Chemistry," Interscience Publ. Inc., New York, 1956, Vol. IX, pp. 298—299, 471.
[14] Bladé-Font, VanderWerf, and McEwen, *J. Amer. Chem. Soc.*, 1960, **82**, 2396, giving further references.

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C, 62·9; H, 4·4; Cl, 19·4; P, 8·4. Calc. for $C_{18}H_{15}Cl_2OP$: C, 63·1; H, 4·2; Cl, 19·7; P, 8·6%). The P=O band at about 1266 cm.$^{-1}$ was shown by the dichloride already in the crude reaction product (after washing with water and ether; m. p. 140—150°). Rearrangement was therefore not a result of the purification procedure. The infrared absorption spectra of solutions of this material in the sodium chloride range in chloroform (29 mg. + 1 ml.) and carbon disulphide (saturated solution) were measured with a Perkin–Elmer model 12C spectrophotometer. The following major bands were observed (frequencies in cm.$^{-1}$). In $CHCl_3$: 1599m, 1500m, 1442m, (all νC_{Ar}–C_{Ar}), 1255s, (νP=O), 1082w, 1035w, (both in plane νC_{Ar}–H bending), 1002w; (not measured below 830 cm.$^{-1}$). In CS_2 (measured only from 1400 cm.$^{-1}$ downwards): 1266s, (νP=O), 1035w, 735s, 697s, (both out-of-plane νC_{Ar}–H bending).

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THE WEIZMANN INSTITUTE OF SCIENCE,
REHOVOTH, ISRAEL.

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690. *The Biosynthesis of Polyacetylenes. Part IV.* The Rate of Polyacetylene Synthesis by Basidiomycete* B.841.

By J. D. BU'LOCK, H. GREGORY, and M. HAY.

IN comparing different carbon sources for the synthesis of polyacetylene antibiotics by Basidiomycete B.841,[1] ethanol was found to be markedly superior to glucose.[2] A more detailed study was therefore made to determine whether the increased synthesis represented a general acceleration of metabolism or a more efficient use of substrate.

Previous experience has shown that good reproducibility is obtained when B.841 mycelium is grown from visually matched inocula supplied first with a glucose–salts–maize-steep medium, then with 4% (w/v) aqueous glucose, and finally with the experimental medium. In these experiments, such cultures (with identical previous histories) were supplied with either 4% (w/v) glucose or 1·5% (w/v) ethanol, together with tracer amounts of [1-^{14}C]acetate, and the polyacetylene production, substrate consumption, and carbon dioxide release were measured (see Experimental section). All proceeded at uniform rates, given in the Table as mg. of carbon per flask per day.

Substrate	4% (w/v) glucose		1·5% (w/v) ethanol	
	mg. C/flask/day	%	mg. C/flask/day	%
Substrate used	168	(100)	280	(100)
CO_2 released	80	48	152	54
Polyacetylenes (as $C_{11}H_{10}O_3$ *)	7	4	40	14
Xylose combined in polyacetylenes	2	1	10	4
Apparent assimilation (by difference)	79	47	78	28
[1-^{14}C]Acetate incorporated into polyacetylenes		14·8%		15·8%
C_2 turnover (from ^{14}C incorporation)	47	28	252	90

* Cf. nemotinic acid.[1]

In this series, polyacetylene synthesis from ethanol is about six times as rapid as from the glucose (cf. Table). The polyacetylenes are derived from the " acetate " C_2 pool,[3] (probably from acetyl-coenzyme-A) and as shown by the ^{14}C incorporation (cf. Table) the proportion of the C_2 pool used in this way is not affected by the change of substrate. The increased polyacetylene synthesis therefore corresponds to a proportionately increased turnover of precursor " acetate."

The yield of polyacetylenes from ethanol is virtually the same as the percentage incorporation of [1-^{14}C]acetate, *i.e.*, at least 90% of the ethanol consumed is utilised by

* Part III, Bu'Lock, Allport, and Turner, *J.*, 1961, 52.

[1] Bu'Lock and Gregory, *J.*, 1960, 2280.
[2] Bu'Lock and Gregory *Biochim. Biophys. Acta*, 1961, **48**, 406.
[3] Bu'Lock and Gregory, *Biochem. J.*, 1959, **72**, 322.

way of " acetate " (most of the remainder can be accounted for as acetaldehyde). This is clearly not true of the glucose utilisation (cf. Table) since the C_2 turnover (calculated from ^{14}C-incorporation and polyacetylene yield) is only 28% of the glucose-carbon consumed. The polyacetylenes produced (including a small amount of combined xylose [1]) and the carbon dioxide released together account for little more than half of the glucose-carbon consumed, leaving about 47% not accounted for. With ethanol as substrate, about 54% appears as carbon dioxide, 4% as xylose combined with the polyacetylenes, and a remaining 28% is not accounted for (cf. Table).

A careful examination of the culture media from this experiment and from many others has failed to reveal any substances (other than the polyacetylenes, combined xylose, and unused substrate) in amounts sufficient to modify significantly these deficits in the carbon balance, and we conclude that the remaining carbon has been assimilated into the mycelium in the way found in many other fungi.[4] This is not in itself surprising, but it appears somewhat remarkable that, with the two different substrates used, though the proportions assimilated are quite different, the rates of assimilation are virtually the same. From the data, the assimilation of glucose occurs mainly by pathways not involving " acetate," in contrast to the utilisation of ethanol. It appears that once the rates of the assimilatory processes have been established, during the previous history of the mycelial samples, they control the further uptake of substrate, whether glucose or ethanol, and the different turnover of " acetate " required to maintain the assimilation rate in the two cases is directly reflected in different rates of antibiotic synthesis.

Experimental.—General culture conditions and radiochemical techniques were as previously described,[3] and the mixture of polyacetylenes (free and combined as xylosides) was analysed by double solvent extraction and spectrophotometric assay.[1] The glucose content of media was determined by Somogyi's method [5] (after the sample had been boiled for 5 min. to remove interfering polyacetylenes), and ethanol by Fidler's method.[6] Carbon dioxide production was measured by passing CO_2-free air through the flasks and into standardised aqueous barium hydroxide for a measured period each day and titrating the excess of alkali after ½—2 hr. The analyses were carried out on duplicate flasks from a single matched batch, with a total of 10 samples (10 ml. each) from each flask during 20—30 days; the steady rates observed over the greater part of this period are given in the Table as mg. of carbon per flask per day and as % of substrate carbon consumed. The reproducibility of such experiments is within ±5%.

Incorporation of [1-^{14}C]acetate is given as % of administered activity present as polyacetylenes (excluding combined xylose), after incubation in duplicate flasks of the same batch for 10 days with 6 μc of [1-^{14}C]acetate, measured by counting weighed thin films of 4-oxoundecanamide and estimating total polyacetylenes spectrophotometrically.

THE UNIVERSITY, MANCHESTER, 13. [*Received, February 23rd*, 1961.]

[4] Clifton, *Adv. Enzymology*, 1946, **6**, 269.
[5] Somogyi, *J. Biol. Chem.*, 1945, **160**, 69.
[6] Fidler, *Biochem. J.*, 1934, **28**, 1107.

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691. *Gibberellin A_2.*

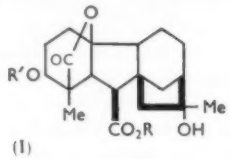
By JOHN FREDERICK GROVE.

BOTH gibberellin A_2 (I; R = R′ = H) [1] and gibberellin A_4 (II; R = R′ = H) [2] have been obtained from certain strains of *Gibberella fujikuroi* and the relation between these two metabolites has been established by Sumiki and his co-workers [3] who obtained acetylgibberellin A_4 methyl ester (II; R = Me, R′ = Ac) by dehydration of acetylgibberellin

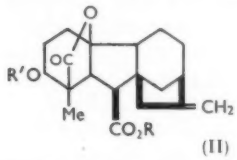
[1] Takahashi, Kitamura, Kawarada, Seta, Takai, Tamura, and Sumiki, *Bull. Agr. Chem. Soc. Japan*, 1955, **19**, 267; Takahashi, Seta, Kitamura, Kawarada, and Sumiki, *ibid.*, 1957, **21**, 75.
[2] Takahashi, Seta, Kitamura, and Sumiki, *Bull. Agr. Chem. Soc. Japan*, 1957, **21**, 396; 1959, **23**, 405.
[3] Kitamura, Takahashi, Seta, and Sumiki, *Bull. Agr. Chem. Soc. Japan*, 1958, **22**, 434.

XUM

A_2 methyl ester (I; R = Me, R′ = Ac) with phosphorus oxychloride in pyridine. The structure of gibberellin A_2 is confirmed by its formation, already briefly reported,[4] when gibberellin A_4 is treated with 3N-hydrochloric acid at room temperature during 2 days.



(I)



(II)

Aqueous solutions of gibberellin A_4 were stable at pH 1·3 for 3 days and at pH 3·2 for 2 weeks as judged by the absence of any change in the ultraviolet end-absorption due to the terminal methylene group. These results make it unlikely that gibberellin A_2 is an artefact, produced from gibberellin A_4, unless very strongly acidic conditions were used [1] during extraction of the fermentation broths.

Gibberellin A_2 showed dimorphism and, in agreement with a recent report,[5] formed a methyl ester $C_{20}H_{28}O_6,H_2O$. The latter was the main product when gibberellin A_4 methyl ester was boiled with dilute mineral acid: two unidentified minor products were also isolated from this reaction. Consistent with structure (I; R = Me, R′ = H) the hydrogen (proton) nuclear magnetic resonance spectrum of gibberellin A_2 methyl ester showed two sharp peaks at $\tau = 8{\cdot}97$ and 8·72 due to the two methyl groups attached to fully-substituted carbon atoms.

Experimental.—M. p.s are corrected. Infrared spectra were determined on Nujol mulls unless stated otherwise. Nuclear magnetic resonance spectra (tetramethylsilane as internal standard with $\tau = 10{\cdot}00$) were obtained in chloroform by Dr. N. Sheppard, University of Cambridge.

Action of hydrochloric acid on gibberellin A_4. (*A*) The acid (30 mg.) in methanol (0·5 ml.) and 3N-hydrochloric acid (2 ml.) was set aside for 2 days at room temperature. After addition of water (1 ml.), the solution was extracted with ethyl acetate, and the product was recrystallised three times from ethyl acetate giving gibberellin A_2 as felted needles (15 mg.), m. p. 255° (decomp.) (Found: C, 65·0; H, 7·35. Calc. for $C_{19}H_{26}O_6$: C, 65·1; H, 7·5%); $\nu_{max.}$ 3470 (sh), 3380 (broad) (OH); 1752, 1708 cm.$^{-1}$ (C=O). The infrared spectrum was unaltered by drying the material at 100° *in vacuo* and was identical with that of an authentic specimen of gibberellin A_2 kindly provided by Prof. Y. Sumiki, University of Tokyo: it differed significantly from the spectrum [1] of the form, m. p. 235—237°.[1] Gibberellin A_2 did not give a colour with concentrated sulphuric acid.

The methyl ester, prepared with diazomethane, crystallised from ethyl acetate in plates or prisms, m. p. 120° and 190°, $[\alpha]_D^{26}$ +25° (*c*, 0·6 in methanol), of the *monohydrate* (Found: C, 63·15; H, 8·0. $C_{20}H_{28}O_6,H_2O$ requires C, 62·8; H, 7·9%); $\nu_{max.}$ 3495, 3350, 3180 (OH); 1760, 1747 (C=O); 1672 cm.$^{-1}$ (H_2O). The infrared spectrum was identical with that of " gibberellin A_2 methyl ester sesquihydrate, m. p. 190—192° $[\alpha]_D$ +28° " [1] now presumably regarded [5] as a monohydrate, and with that of a specimen of the ester obtained by methylation of the authentic specimen of gibberellin A_2. The anhydrous *ester*, m. p. 190°, was obtained by drying the hydrate for 24 hr. *in vacuo* at room temperature over phosphorus pentoxide (Found: C, 66·3; H, 7·8. $C_{20}H_{28}O_6$ requires C, 65·9; H, 7·7%); $\nu_{max.}$ 3570; 1733 cm.$^{-1}$ [1770 (γ-lactone C=O) in dioxan]. The infrared spectrum was identical with that of gibberellin A_2 methyl ester.[1]

(*B*) A solution of the acid (5·3 mg.) in ethanol (0·5 ml.) and water (49·5 ml.) was adjusted to pH 3·2 with hydrochloric acid and set aside at room temperature. The ultraviolet absorption from 200 to 250 mμ was measured at intervals. No changes were recorded after 2 weeks. Similarly, no changes were observed during 5 days at pH 2·3 and during 3 days at pH 1·3. Gibberellin A_4 was recovered by extraction with ethyl acetate and identified by the infrared spectrum.

[4] Brian, Grove, and MacMillan, *Fortschr. Chem. org. Naturstoffe*, 1960, **18**, 350.
[5] Kitamura, Seta, Takahashi, Kawarada, and Sumiki, *Bull. Agr. Chem. Soc. Japan*, 1959, **23**, 408.

XUM

ε at 205 mμ for gibberellin A_4 in ethanol–3N-hydrochloric acid (1 : 1) fell from an initial value of 7950 to 5700 after 2·5 hr. and to 2100 after 19 hr.

Action of sulphuric acid on gibberellin A_4 methyl ester. The ester (70 mg.) was heated under reflux in methanol (2 ml.) and 3N-sulphuric acid (4 ml.) in a stream of nitrogen for 1 hr. Carbon dioxide was not evolved. After removal of methanol by distillation *in vacuo* the residual solution was extracted with ethyl acetate, and the extract was washed with sodium hydrogen carbonate and recovered. The neutral product (59 mg.) was chromatographed in benzene–methanol (200 : 1, 200 ml.) on alumina (Grade II; pH 4; 10 × 0·7 cm.) by fractional elution [50 ml. fractions of benzene–methanol (200 : 1)]. The gummy products (weights in parentheses) were crystallised from ethyl acetate–light petroleum (b. p. 60—80°): (i) (8 mg.) microprisms, m. p. 120—130°; $\nu_{max.}$ 3485 (OH); 1773, 1737 (weak), 1712 (C=O); 1653 cm.$^{-1}$. (ii) (7 mg.) intractable. (iii)—(x) (39 mg.) gibberellin A_2 methyl ester, m. p. 188—190°. (xi)—(xiv) (6 mg.) prisms of a *substance*, m. p. 155—157° (Found: C, 60·2; H, 8·0. $C_{20}H_{28}O_6,2H_2O$ requires C, 60·0; H, 8·05%); $\nu_{max.}$ 3500, 3395, 3155 (OH); 1756, 1726 (C=O); 1645 cm.$^{-1}$.

IMPERIAL CHEMICAL INDUSTRIES LIMITED, AKERS RESEARCH LABORATORIES,
THE FRYTHE, WELWYN, HERTS. [*Received, March 1st,* 1961.]

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692. *The Thermal Unimolecular Isomerisation of Vinylcyclopropane to Cyclopentene.*

By M. C. FLOWERS and H. M. FREY.

CYCLOPROPANE and alkylcyclopropanes readily undergo thermal unimolecular isomerisation to olefins.[1] The rate equations of these reactions are characterised by high pre-exponential factors that can be accounted for, in part, by an entropy increase in the transition state due to ring opening. It seemed possible that vinylcyclopropane might undergo another type of isomerisation, to give cyclopentene. This reaction would involve no hydrogen shifts (which occur in the normal cyclopropane isomerisations); and, further, if the transition state involves simultaneous rupture of the three-membered ring and formation of the five-membered ring, little entropy increase in this transition state would be expected.

Vinylcyclopropane has been found to undergo a first-order thermal isomerisation to cyclopentene, which is almost certainly truly unimolecular, in the temperature range 339—391° c. This reaction has been investigated at four temperatures in this range and a good Arrhenius plot obtained, from which $k = 10^{13.5} \exp(-49{,}600/RT)$ sec.$^{-1}$. The "normal" value of the pre-exponential factor is clearly consistent with the transition state suggested above. Further, the low value of the energy of activation also indicates that the new carbon–carbon bond is being formed simultaneously with the rupture of the cyclopropane ring. At the highest temperature investigated (390·5° c) approximately 1·0% of the product was a mixture of penta-1,4-diene, isoprene, and *cis*- and *trans*-penta-1,3-diene. These products arise from the "normal" cyclopropane isomerisation, where shift of a hydrogen atom occurs with the ring rupture. The very small quantities of these dienes are to be expected from the much higher energy of activation of such cyclopropane isomerisations.

Experimental.—Vinylcyclopropane was prepared by photolysis of a gaseous mixture of keten and buta-1,3-diene at 1000 mm. at room temperature. The vinylcyclopropane was separated from the complex mixture by gas chromatography and stored as a gas at low pressure. The thermal isomerisation was carried out in a 1·4-l. Pyrex vessel contained in a horizontal furnace whose temperature was maintained within ±0·1°. Mercury cut-offs and Polythene or Fluon diaphragm valves were used, to avoid absorption associated with the use of conventional vacuum-stopcocks. The products were analysed by gas chromatography. With a 25 ft.

[1] W. E. Falconer, T. F. Hunter, and A. F. Trotman-Dickenson, *J.*, 1961, 609; J. P. Chesick, *J. Amer. Chem. Soc.*, 1960, **82**, 3277; M. C. Flowers and H. M. Frey, *J.*, 1959, 3953; M. C. Flowers and H. M. Frey, *Proc. Roy. Soc.*, 1960, *A*, **257**, 122.

XUM

column containing 40—60 mesh Chromosorb with 15% by weight of acetonylacetone maintained at 0°, and with a flow rate of about 50 ml. of hydrogen per minute, cyclopentene was eluted in 40 min. and vinylcyclopropane in 63 min. A Gow–Mac tungsten-filament katharometer was used as a detector, and the signal fed to a 1 mv recorder fitted with a retransmitting slide-wire. The signal from the second slide-wire was used to operate a Perkin–Elmer model 194 integrator. Peak areas for mixtures of cyclopentene and vinylcyclopropane were found to be directly proportional to their mole percentages. The reproducibility of duplicate analyses was better than 0·5%.

The identification of all peaks was by time of elution from the chromatographic column, compared with those of the pure compounds. The major peaks were each confirmed as being due to only one component by mass spectrometry.

One of us (M. C. F.) thanks the Esso Petroleum Company for the award of a research studentship. The other (H. M. F.) thanks the Royal Society and the Department of Scientific and Industrial Research for grants for apparatus.

Department of Chemistry, University of Southampton. [*Received, March 7th*, 1961.]

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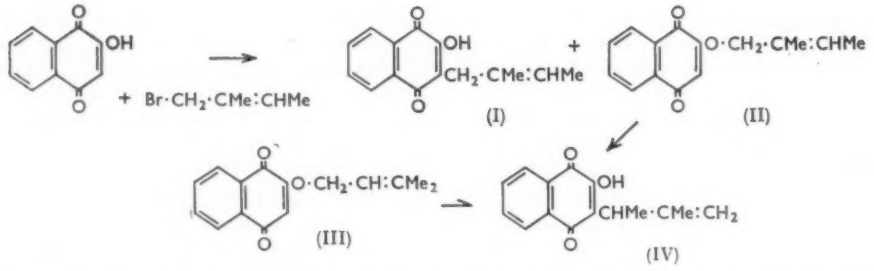
693. *A New Synthesis of Isodunniol.*

By R. I. T. Cromartie and P. M. Scott.

Isodunniol was first obtained by Price and Robinson [1] by a series of reactions from the natural pigment dunnione. The formula (IV) was proposed for it by Cooke and Somers [2] although it involved a shift of the double bond out of conjugation with the aromatic ring, and Cooke [3] synthesised the quinone by an abnormal Claisen rearrangement of the allyl ether (III).



The formula (IV) for isodunniol has now been confirmed by synthesis by normal Claisen rearrangement of the allyl ether (II), which was obtained, together with the corresponding *C*-alkyl derivative (I), by reaction of 2-methylbut-2-enyl bromide with the silver salt of 2-hydroxy-1,4-naphthaquinone. The synthetic material was identical with the original specimen of Price and Robinson, of which Dr. R. G. Cooke kindly sent us a sample.

Experimental.—Reaction of 2-hydroxy-1,4-naphthaquinone with 2-methylbut-2-enyl bromide. The silver salt of 2-hydroxy-1,4-naphthaquinone (10·8 g.) was added in portions during 1 hr. to the bromide [4] (6·2 g.) in benzene (50 c.c.), and the mixture was stirred for 8 hr., filtered, shaken with 2% sodium hydroxide solution, and evaporated. The residue was recrystallized from benzene–light petroleum (b. p. 60—80°), sublimed at 90°/10^{-4} mm., and again recrystallized from ether–light petroleum (b. p. 40—60°), yielding 2-(*2-methylbut-2-enyloxy*)-1,4-*naphthaquinone* as pale yellow needles, m. p. 127—128° (Found: C, 74·1; H, 6·1. $C_{15}H_{14}O_3$ requires

[1] Price and Robinson, *J.*, 1940, 1493.
[2] Cooke and Somers, *Austral. J. Sci. Res.*, 1950, *A***3**, 466.
[3] Cooke, *Austral. J. Sci. Res.*, 1950, *A***3**, 481.
[4] Lauchenauer and Schinz, *Helv. Chim. Acta*, 1951, **34**, 1514.

C, 74·4; H, 5·8%), $\lambda_{max.}$ (in EtOH) 243, 248, 276, and 330 mμ (log ε 4·27, 4·30; 4·16, and 3·44 respectively), $\nu_{max.}$ (mull) 668, 720, 781, 817, 870, 948, 1007, 1028, 1050, 1088, 1120, 1214, 1257, 1313, 1337, 1363, 1444, 1582, 1598, 1610, 1652, 1683, 2860, 2920, and 3050 cm.$^{-1}$.

Acidification, with acetic acid, of the alkaline extract obtained above precipitated 2-hydroxy-3-(2-methylbut-2-enyl)-1,4-naphthaquinone (1·6 g.), which after recrystallization from aqueous acetic acid (charcoal) and then from ether–light petroleum (b. p. 40—60°) had m. p. 122—123·5° (lit.,[5] 123·5—124·5°).

The hydroxyquinone with zinc dust, acetic anhydride, and pyridine furnished 1,2,4-*triacetoxy*-3-(2-*methylbut*-2-*enyl*)*naphthalene* needles (from aqueous acetone), m. p. 162—164° (Found: C, 68·1; H, 6·2. $C_{21}H_{22}O_6$ requires C, 68·1; H, 6·0%).

Isodunniol. The ether (II) (1·6 g.) was boiled for 1 min. with glacial acetic acid (20 c.c.). The solution was diluted with water (20 c.c.), cooled, filtered to remove unchanged starting material, and further diluted with water (50 c.c.). Isodunniol separated gradually as yellow needles, which after two recrystallizations from aqueous ethanol and sublimation at 100°/10^{-3} mm. had m. p. 116—119° (lit.,[3] 119°) undepressed on admixture with natural isodunniol (Found: C, 74·4; H, 6·1. Calc. for $C_{15}H_{14}O_3$: C, 74·4; H, 5·8%). The infrared spectra (KBr disc) of the synthetic and the natural compound were identical, showing maxima at 729, 800, 871, 886, 946, 975, 1007, 1030, 1051, 1079, 1094, 1163, 1180, 1210, 1235, 1280, 1351, 1375, 1467, 1593, 1629, 1655, 2940, 2985, and 3350 cm.$^{-1}$.

One of us (P. M. S.) thanks the Department of Scientific and Industrial Research for a Maintenance Award.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, March 15th,* 1961.]

[5] Gates and Moesta, *J. Amer. Chem. Soc.*, 1948, **70**, 614.

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694. *Fluorination of the Trioxides of Chromium, Molybdenum, Tungsten, and Uranium by Selenium Tetrafluoride.*

By NEIL BARTLETT and P. L. ROBINSON.

SELENIUM TETRAFLUORIDE can act as a fluorinating agent by exchanging fluorine for oxygen. Thus selenium oxyfluoride is most conveniently prepared by the reaction:[1] $SeF_4 + SeO_2 \longrightarrow 2SeOF_2$. Again, when selenium tetrafluoride attacks glass,[2] a similar exchange occurs: $SeF_4 + SiO_2 = SeO_2 + SiF_4$. The best method[3] of making tellurium tetrafluoride is by the reaction: $2SeF_4 + TeO_2 = 2SeOF_2 + TeF_4$. With vanadium pentoxide, the complex oxyfluoride $(SeF_4)_2VOF_3$ is formed.[2]

We have investigated the reactions between selenium tetrafluoride and the transition-metal trioxides of Group VI. Iodine pentafluoride has similar fluorinating properties as its behaviour with three of these trioxides shows.[4]

Reactions of SeF_4 *and* IF_5 *with Group* VIA *Trioxides.*

Oxide	Reaction with SeF_4	Reaction with IF_5
CrO_3	$CrO_3 + SeF_4 \longrightarrow CrO_2F_2 + SeOF_2$	$2CrO_3 + IF_5 \longrightarrow 2CrO_2F_2 + IO_2F$
MoO_3	$MoO_3 + 2SeF_4 \longrightarrow SeF_4,MoO_2F_2 + SeOF_2$	$2MoO_3 + 3IF_5 \longrightarrow 2IF_5,MoO_2F_2 + IO_2F$
WO_3	$WO_3 + 3SeF_4 \longrightarrow SeF_4,WOF_4 + 2SeOF_2$	$WO_3 + 2IF_5 \longrightarrow IF_5,WOF_4 + IO_2F$
	$WO_3 + 2SeF_4 \longrightarrow SeOF_2,WOF_4 + SeOF_2$	
UO_3	$UO_3 + SeF_4 \longrightarrow UO_2F_2 + SeOF_2$	
	$UO_2F_2 + SeF_4 \longrightarrow UOF_4 + SeOF_2$	

Chromyl fluoride does not form a complex with either selenium tetrafluoride or iodine pentafluoride, although the oxyfluoride dissolves freely in each. It is probable that the quinqueco-ordinate ion, $CrO_2F_3^-$, is too unstable. The molybdenum complex $SeMoO_2F_6$

[1] Aynsley, Peacock, and Robinson, *J.*, 1952, 1231.
[2] Peacock, *J.*, 1953, 3617.
[3] Campbell and Robinson, *J.*, 1956, 785.
[4] Aynsley, Nichols, and Robinson, *J.*, 1953, 623.

XUM

could be formulated as either SeF_4,MoO_2F_2 or $SeOF_2,MoOF_4$; the latter is, however, unlikely since $KMoOF_5$ is not produced by equimolecular quantities of potassium fluoride and molybdenum trioxide in selenium tetrafluoride. The complex oxyfluoride $KWOF_5$ is formed in the reaction, $KF + WO_3 + 2SeF_4 \longrightarrow KWOF_5 + 2SeOF_2$. In the absence of potassium fluoride, the product may be a mixture of SeF_4,WOF_4 and $SeOF_2,WOF_4$.

Experimental.—Reactions with selenium tetrafluoride. (1) Chromium trioxide (1 g.) was warmed to 40° with selenium tetrafluoride (20 ml.), to give a bright red solution over which was brown chromyl fluoride vapour. Polymerisation of the chromyl fluoride was not observed; its vapour condensed to a red-brown solid (Found: Cr, 41·9; F, 32·1. Calc. for CrO_2F_2: Cr, 42·6; F, 31·2%). When the excess of selenium tetrafluoride and other material volatile at 0° were pumped from the reaction bub, the white residue, m. p. 15°, was selenium oxyfluoride and there was no evidence of the formation of a complex compound.

(2) Molybdenum trioxide (1·5 g.) dissolved in selenium tetrafluoride (10 ml.) at 50°; the straw-coloured solution deposited colourless crystals on cooling. These were recovered by removing the excess of selenium tetrafluoride and other volatile materials under a vacuum at 18°. They melted at 71—72°, distilled unchanged under a vacuum, and reacted violently with water. A solution of the substance in sodium hydroxide was acidified with hydrochloric acid, and the selenium precipitated with sulphurous acid. It was washed with concentrated ammonia solution (to remove any molybdic acid) then with water, alcohol, and ether. Fluorine was determined as lead chloride fluoride in the fluorosilicic acid–hydrofluoric acid distillate from a water–sulphuric acid mixture boiling at 132—138°. Molybdenum was precipitated as oxine complex. The *product* had composition SeF_4,MoO_2F_2 (Found: Se, 25·5; F, 35·4; Mo, 28·2. SeF_4,MoO_2F_2 requires Se, 24·6; F, 35·5; Mo, 29·9%).

(3) Equimolecular quantities of molybdenum trioxide and potassium fluoride were mixed and dissolved in boiling selenium tetrafluoride. White crystals separated on cooling, from which the excess of selenium tetrafluoride was removed under a vacuum at 70°. The solid was difficult to free from solvent and readily absorbed selenium tetrafluoride vapour. It dissolved easily in water to give a colourless solution. Qualitative analysis showed the presence of much combined selenium, and an *X*-ray powder photograph showed that it was a mixture containing the SeF_4,MoO_2F_2 phase.

(4) Tungsten trioxide (1·2 g.) was refluxed in selenium tetrafluoride (20 ml.) for 15 min. and gave a pale yellow, slightly opalescent solution. Removal of the selenium tetrafluoride under a vacuum at room temperature left a yellow solid, m. p. 60—63°, which dissolved quietly in water. Selenium and fluorine were determined as described. The tungstic acid which separated with the selenium was washed from it with concentrated aqueous ammonia, precipitated as the cinchonine salt, and ignited to tungsten trioxide. The product (Found: Se, 17·2; F, 28·8; W, 43·0. Calc. for SeF_4,WO_2F_2: Se, 19·3; F, 27·8; W, 43·0. Calc. for SeF_4,WOF_4: Se, 18·3; F, 35·3; W, 42·7%) is probably SeF_4,WO_2F_2 mixed with a smaller quantity of SeF_4,WOF_4. The combined yield (1·5 g.) was low and it is probable that a volatile colourless compound of tungsten distilled with the selenium tetrafluoride since tungsten was present in the latter.

(5) Equimolecular proportions of tungsten trioxide and potassium fluoride were dissolved in boiling selenium tetrafluoride to give an off-white precipitate on cooling. Selenium tetrafluoride and volatile products, when removed under a vacuum at 140°, left a pale buff solid. This dissolved slowly in water to a colourless solution from which tungstic acid separated on acidification (Found: F, 28·7; W, 53·6. Calc. for $KWOF_5$: F, 28·4; W, 55·1%).

(6) Uranium trioxide (0·8 g.) was refluxed with selenium tetrafluoride (20 ml.) for 30 min. during which the oxide changed to a cream-coloured solid. Selenium tetrafluoride was removed under a vacuum at 120°. The solid dissolved quietly in water to a light green solution from which selenium was absent. Uranium was determined as oxinate and fluorine as lead chlorofluoride. The product (Found: F, 21·6; U, 73·5. Calc. for UO_2F_2: F, 12·3; U, 77·3. Calc. for UOF_4: F, 23·0; U, 72·1%) was probably incompletely fluorinated uranium oxytetrafluoride.

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695. *An Examination of the Rutaceae of Hong Kong. Part VII.* The Essential Oils.*

By H. R. Arthur, S. W. Tam, and (in part) (Miss) Y. L. Ng.

Essential oils of seven species of the Hong Kong Rutaceae have been examined, mainly by gas chromatography. The results are recorded in the Table.

Plant species [a]	Constituents of oils
Acronychia pedunculata	α-Pinene; limonene
Evodia lepta	α-Pinene; furfuraldehyde
Fortunella hinsii	Furfuraldehyde
,, , berries	α-Pinene, limonene, *p*-cymene
Ruta graveolens	Methyl nonyl ketone
Zanthoxylum avicennae	α-Pinene, limonene, furfuraldehyde
Z. cuspidatum	Furfuraldehyde
Z. nitidum	Limonene, furfuraldehyde
	Other constituents
A. pedunculata, heartwood	β-Sitosterol
Z. cuspidatum, root bark	Nitidine

[a] Leaves, unless otherwise stated.

Previous work appears not to have been done on the essential oils of the genera *Acronychia* and *Fortunella*. Our work has not revealed in them constituents other than those reported previously from Rutaceae oils. The oils from the *Evodia*, the *Ruta*, and the three *Zanthoxylum* species, now examined for the first time, contain constituents also commonly found in Rutaceae oils. A minor unidentified compound has been detected as a constituent in five of the oils: it is only present when furfuraldehyde also occurs.

The constituents named were first tentatively identified by comparing their retention times in the gas chromatogram with those of authentic samples: then identity was confirmed by gas chromatography of samples to which the authentic substance had been added.

Limonene and α-pinene are present in about equal amount in *A. pedunculata* oil. Methyl nonyl ketone, previously reported to be the chief constituent of many *Ruta* species, was considered to be present in the oil of *Ruta graveolens* because of its odour and because the infrared spectrum of the oil showed strong absorption at 1720 cm.$^{-1}$ (stretching frequency for $\rangle$C=O); it was identified by conversion into the semicarbazone and the 2,4-dinitrophenylhydrazone; the chromatogram showed that this ketone constituted nearly the whole of this oil.

The leaves and stem bark of *Acronychia pedunculata* gave weak positive tests with alkaloid reagents. A preliminary examination, however, suggests that they are present at most in low yield, as seems to be the case for many of the Australian *Acronychias*.[1] The heartwood of this plant yielded " β "-sitosterol. The root bark of *Zanthoxylum cuspidatum* was shown to contain nitidine (which was reported [2] to occur in *Z. nitidum*) by conversion of the crude alkaloid salts into dihydronitidine and oxynitidine.

Experimental.—Chromatograms were taken on a Pye " Argon Chromatograph," spectra on a Perkin–Elmer Infracord (model 137) spectrophotometer, and m.p.s on a Kofler block. Light petroleum refers to the fraction of b. p. 40—60°. Microanalyses were made by Dr. K. W. Zimmermann, Melbourne.

Essential oils. (*a*) Isolation. Fresh leaves (about 100 g.) of all plant species were steam-distilled and the distillate was extracted repeatedly with chloroform. The chloroform extract was dried (Na_2SO_4). Removal of the solvent gave a pale yellow oil (about 0·5 ml.). Berries were crushed, then treated as for leaves to obtain the oil. The oil from the leaves of *Acronychia*

* Part VI, *Austral. J. Chem.*, 1960, **13**, 510.

[1] Webb, C.S.I.R.O. (Australia), Bull. 241 (1949), 268 (1952).

[2] Arthur, Hui, and Ng, *J.*, 1959, 1840.

XUM

pedunculata was, for comparison, also obtained as follows: air-dried leaves were extracted with light petroleum for 10 days. Removal of the solvent from this extract left a brown tar which was steam-distilled. The distillate was extracted with light petroleum. The petroleum extract was dried and distilled. A yellow oil was obtained.

(*b*) Chromatography. Glass columns (length, 4 ft.; int. diam., 4—5 mm.) were used. Apiezon L grease (as stationary phase) (to give 20% w/w with Celite) was dissolved in light petroleum and the solution was stirred with Celite 545 (mesh 80—120). The petroleum was removed on the steam-bath, with stirring, and the residue was dried in the oven at 100°.

Argon pressure at inlet was 12 lb./sq. in. Exit pressure was atmospheric. The gas flow was kept constant at 10 ml./35 sec. measured with a soap-bubble flow indicator. The temperature was 150°. The ionisation detector voltage was 1000—1500 v.

Micropipettes (0·05 μl. or 0·10 μl.) were filled with oil by capillary attraction. The argon flow was stopped, then after 30 sec., the column connector tube was removed and the sample was injected. Authentic samples were added to oils by first dipping the micropipette into the oil, and then, for a short time, into the authentic sample.

(*c*) Results. Retention times, measured from the starting point of the negative air peak, were as follows: furfuraldehyde, 6·5; α-pinene, 13·9; limonene, 24·7; *p*-cymene, 22·8; methyl nonyl ketone, 23·6 min. (all measured on one column under the same conditions). Methyl nonyl ketone was identified by conversion into (i) the semicarbazone (from 0·2 g. of oil, 0·3 g. of sodium acetate, and 0·2 g. of semicarbazide hydrochloride, boiled under reflux in aqueous ethanol for 5 min.) which crystallised from aqueous methanol and had m. p. 121—122°, and (ii) the 2,4-dinitrophenylhydrazone (obtained from the oil and an acidic solution of the reagent), m. p. 62—63° (from aqueous methanol).

Other compounds. (*a*) From *Acronychia pedunculata*. Chopped air-dried heartwood (1·5 kg.) was extracted with methanol (17 l.) (Soxhlet) for 24 hr. The extract was concentrated to 0·5 l. After 2 days, a first, then a second, small crop of pale green solid were collected. They were combined and crystallised three times from methanol (charcoal). " β "-Sitosterol separated as plates (0·045 g., 0·003%), m. p. and mixed m. p. 138—140°, $[\alpha]_D$ −42·1° (*c* 1·0 in $CHCl_3$) (Found: C, 82·4; H, 12·1. Calc. for $C_{29}H_{50}O$: C, 84·0; H, 12·2%). The infrared spectrum taken in Nujol was identical with that of authentic " β "-sitosterol. This compound was characterised as the acetate (acetic anhydride and pyridine), m. p. 128—130° (from methanol).

(*b*) From *Zanthoxylum cuspidatum* (with Miss Y. L. Ng). Milled air-dried root bark (3 kg.) was extracted with hot methanol (17 l.) (Soxhlet) for 30 hr. The extract was concentrated to 0·5 l. After a few days yellow crystals (4·5 g.) were collected. Decomposition of the salts and then treatment with hot aqueous ammonia (disproportionation) gave a mixture which after chromatography and recrystallisation of the fractions as stated for *Z. nitidum* [2] yielded dihydronitidine, m. p. and mixed m. p. 221—223° (Found: C, 72·9; H, 5·7; N, 4·2. Calc. for $C_{21}H_{19}NO_4$: C, 72·2; H, 5·4; N, 4·0%), and oxynitidine, m. p. and mixed m. p. 284—285° (Found: C, 69·2; H, 4·7; N, 4·0. Calc. for $C_{21}H_{17}NO_5$: C, 69·4; H, 4·7; N, 3·9%).

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